Medtronic

Surgical Innovations
Lung Health
161 Cheshire Lane
Suite 100
Plymouth, MN 55441
USA
www.medtronic.com

Document Cover Page

Study: NAVABLATE

Official Title: Clinical description of a bronchoscopic approach to ablate lung nodules using the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology

ClinicalTrials.gov ID: NCT03569111

Document Type: Study Protocol

Document Date: 26-SEP-2019 (Version 4.0)

Medtronic

Clinical Investigation Plan

Clinical Investigation Plan/Study Title	Clinical description of a bronchoscopic approach to ablate lung nodules using the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology
Clinical Investigation Plan Identifier	MDT18010ILSBA
Study Product Name	Emprint™ Ablation Catheter Kit with Thermosphere™ Technology
Sponsor/Local Sponsor	Medtronic Minimally Invasive Therapies Group Surgical Innovations, Lung Health 161 Cheshire Lane, Suite 100 Plymouth, MN 55441 Covidien Services Europe (an indirect, wholly owned subsidiary of Medtronic plc) Block 3090-3094 Lake Drive Citywest Business Park Dublin, Ireland
Document Version	Version 4.0, 26-SEP-2019
Lead Principal Investigators	Kelvin K.W. Lau, MA, DPhil, FRCS(CTh) St Bartholomew's Hospital West Smithfield, London EC1A 7BE
	Calvin Ng, BSc MB BS MRCS FRCSEd MD FCSHK FHKAM FCCP Prince of Wales Hospital 30-32 Ngan Shing St, Sha Tin Hong Kong

1. Investigator Statement

Study Product Name	Emprint™ Ablation Catheter Kit with Thermosphere™ Technology
Sponsor/Local Sponsor	Medtronic Minimally Invasive Therapies Group Surgical Innovations, Lung Health 161 Cheshire Lane, Suite 100 Plymouth, MN 55441 Covidien Services Europe (*an indirect, wholly owned subsidiary of Medtronic plc)* Block 3090-3094 Lake Drive Citywest Business Park Dublin, Ireland
Clinical Investigation Plan Identifier	MDT18010ILSBA
Version Number/Date	Version 4.0, 26-SEP-2019
I have read the protocol, including all appendices, and I agree that it contains all necessary details for me and my staff to conduct this study as described. I will conduct this study as outlined herein and will make a reasonable effort to complete the study within the time designated. I agree to comply with ISO 14155:2011 (Clinical Investigation of Medical Devices for Human Subjects – Good Clinical Practice), the European Union Medical Device Regulation, and the International Conference on Harmonisation (ICH) of Technical Requirements For Registration of Pharmaceuticals For Human Use, ICH Harmonised Tripartite Guideline for Good Clinical Practice E6 (R1). I agree to ensure that the confidential information contained in this document will not be used for any purpose other than the evaluation and conduct of the clinical investigation without the prior written consent of Medtronic. I will provide all study personnel under my supervision copies of the protocol and access to all information provided by Medtronic. I will discuss this material with them to ensure that they are fully informed about the products and the study.	
Investigator's Signature:	
Investigator's Name:	
Institution:	
Date:	

Table of Contents

2. Glossary

2.1. Terms

Acronym / Term	Definition
ADE	adverse device effect
ADL	activities of daily living
AE	adverse event
CBCT	cone-beam computed tomography
CIP	clinical investigation plan
CRF	case report form
CT	computed tomography
CTCAE	Common Terminology Criteria for Adverse Events
EC	ethics committee
ENB	electromagnetic navigation bronchoscopy
EU MDR	European Union Medical Device Regulation
EWC	extended working channel
GCP	good clinical practice
GOLD	Global Initiative for Chronic Obstructive Lung Disease
ICF	informed consent form
ICH	International Conference on Harmonisation
IFU	Instructions for Use
IRB	institutional review board
ISO	International Organization for Standardization
IV	intravenous
MHLW	Ministry of Health, Labour, and Welfare
PMV	post-market vigilance
RDC	remote data capture
SADE	serious adverse device effect
SAE	serious adverse event
SAP	statistical analysis plan
SBRT	stereotactic body radiation therapy
USADE	unanticipated serious adverse device effect

2.2. Definitions

Refer to the NAVABLATE Adverse Event Reference List (Appendix 17.5) for additional definitions.

Adverse Event

See Section 11.1.1.

Adverse Device Effect

See Section 11.1.3.

Common Terminology Criteria for Adverse Events

A set of criteria for the standardized classification of adverse effects of drugs used in cancer therapy. The CTCAE system is a product of the US National Cancer Institute Cancer Therapy Evaluation Program.[1] This study will use Version 5.0 (published 27-NOV-2017), available at https://ctep.cancer.gov/protocolDevelopment/electronic_applications/ctc.htm#ctc_50https://ctep.cancer.gov/protocolDevelopment/electronic_applications/ctc.htm#ctc_50

Device Deficiency

See Section 11.1.6.

Instrumental Activities of Daily Living

For the purpose of defining CTCAE grade, instrumental activities of daily living (ADL) refers to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.

Investigational Medical Device

For the purpose of this clinical investigation plan, an Investigational Medical Device is defined as, “A device, including a transitional device, which is the object of an investigation.” The Investigational Medical Device being evaluated in this study is the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology which has received the CE-Mark.

Serious Adverse Device Effect

See Section 11.1.4.

Serious Adverse Event

See Section 11.1.2.

Self-Care Activities of Daily Living

For the purpose of defining CTCAE grade, self-care activities of daily living (ADL) refer to bathing, dressing and undressing, feeding self, using the toilet, taking medications, and not bedridden.[1]

Technical Success

An evaluation of whether the lung nodule was treated according to the study protocol as determined at the immediate post-procedural timepoint. This is in contrast to procedures in which the protocol could not be executed completely, either for technical reasons or for reasons related to comorbid disease.[2]

Technique Efficacy

An evaluation of whether the lung nodule was effectively ablated. Evaluates whether complete ablation of the nodule was achieved as evidenced by imaging follow-up 1-month post-procedure (including a window of 20-40 days post-procedure).[2]

Unanticipated Serious Adverse Device Effect

See Section 11.1.5.

3. Synopsis

Title	Clinical description of a bronchoscopic approach to ablate lung nodules using the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology
Clinical Study Type	Prospective, single-arm, multicenter, non-randomized
Study Phase	Post-market
Product Name	Emprint™ Ablation Catheter Kit with Thermosphere™ Technology
Sponsor/Local Sponsor	Medtronic Minimally Invasive Therapies Group Surgical Innovations, Lung Health 161 Cheshire Lane, Suite 100 Plymouth, MN 55441 Covidien Services Europe (*an indirect, wholly owned subsidiary of Medtronic plc)* Block 3090-3094 Lake Drive Citywest Business Park Dublin, Ireland
Indications for Use/Intended Use Under Investigation	Indications for Use: The Emprint™ Ablation System with Thermosphere™ Technology is intended for use in percutaneous, laparoscopic, endoscopic, and intraoperative coagulation (ablation) of soft tissue, including partial or complete ablation of non-resectable liver tumors. The Emprint™ Ablation System with Thermosphere™ Technology is not intended for use in cardiac procedures. Intended Use: The Emprint™ Ablation Catheter Kit with Thermosphere™ Technology is designed for use with the Emprint™ Ablation System and is compatible with superDimension™ Navigation System's Extended Working Channel (EWC) and Edge™ Bronchoscope Adapter. In this study, the flexible Emprint™ Ablation Catheter will be deployed bronchoscopically using the superDimension™ Navigation System's EWC in order to ablate lung nodules.

	Devices will be used within approved intended use as described in the approved Instructions for Use (IFU) for which CE mark has been obtained per country.
Investigation Purpose	The purpose of this investigation is to characterize the safety and performance of the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology in clinical use.
Product Status	The Emprint™ Ablation Catheter Kit with Thermosphere™ Technology is CE marked and approved for use in each country.
Primary Objective	The primary objective of this prospective, single-arm, multicenter, non-randomized study is to characterize the safety of the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology device in subjects undergoing lung ablation procedures. The primary endpoint is the composite rate of adverse events related to the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology through 1-month follow-up.
Secondary Objectives	The following secondary endpoints will be evaluated: • Composite rate of serious adverse events related to the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology through 1-month follow-up. • Composite rate of all adverse events related to the procedure or study devices through 1-month follow-up. • Composite rate of all serious adverse events related to the procedure or study devices through 1-month follow-up. • Patient satisfaction and pain (Bronchoscopic Ablation Patient Pain and Satisfaction Survey) • Quality of life (EQ-5D Scale) • Technical success • Technique efficacy
Safety Assessments	For safety reporting, only adverse events related to the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology, accessory devices, or study procedures will be captured and reported until the subject exits the study. Adverse events will be summarized as event counts and percentages that occurred during the ablation procedure or were detected after the procedure. For the primary endpoint, relationship specifically to the Emprint™ Ablation Catheter with Thermosphere™ Technology device will be assessed.

	All adverse events related to the Emprint™ Ablation Catheter with Thermosphere™ Technology will be graded for severity based on the Common Terminology Criteria for Adverse Events.[1]
Study Design	This is a prospective, single-arm, multicenter, non-randomized study. Up to 3 sites in up to 3 countries will enroll up to 30 subjects in total. The study is designed to characterize the safety and performance of the bronchoscopic ablation procedure using the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology.
Randomization	This study is not randomized.
Sample Size	Up to 30 subjects will be enrolled at up to 3 sites in up to 3 countries.
Inclusion/Exclusion Criteria	Inclusion Criteria: 1. Subject is ≥ 18 years of age 2. Subject has provided informed consent 3. Subject is able and willing to comply with the study follow-up schedule 4. Subject has a definitive diagnosis of cancer in the lung 5. Target nodule is ≤ 30mm in maximum diameter 6. There is ≥ 5mm of nodule-free lung parenchyma between target nodule and pleura or fissure 7. Subject is a candidate for an elective electromagnetic navigation bronchoscopy (ENB) procedure 8. Subject is a candidate for an elective lung ablation procedure according to standard of care and product Instructions for Use 9. Subject is not a candidate for lung surgery or refuses lung surgery 10. Subject is not a candidate for stereotactic body radiation therapy (SBRT) or refuses SBRT Exclusion Criteria: 1. Target nodule is abutting main stem bronchus, main pulmonary vasculature, esophagus and/or trachea 2. Patients currently diagnosed with Global Initiative for Chronic Obstructive Lung Disease (GOLD) Stage IV emphysema 3. Female subjects who are pregnant or nursing as determined

	by standard site practices 4. Subject has participated in an investigational drug or device research study within 30 days of enrollment that would interfere with this study 5. The investigator determines that participation in the study may jeopardize the safety or welfare of the subject
Study Procedures and Assessments	Subjects will be evaluated at: • Baseline: To determine study eligibility and collect baseline information (demographics, medications, medical history, etc.), Quality of Life Evaluation (EQ-5D scale) • Procedure: To re-confirm nodule eligibility criteria, and collect nodule characteristics, medication changes, procedure plan and procedure information, standard imaging, immediate post-procedure evaluation, adverse event evaluation • 1-month follow-up (20-40 days post-procedure): Standard imaging, follow-up evaluation, medication changes, adverse event evaluation, Bronchoscopic Ablation Patient Satisfaction and Pain Survey, Quality of Life Evaluation (EQ-5D scale)
Statistics	No formal sample size estimates were conducted. Based on the design and purpose of the study, there is no required number of subjects to prove study claims or objectives. The study is predefined to include up to 30 subjects with 20 being the approximate minimum. Study data will be summarized as descriptive statistics (frequencies and percentages) and will inform future studies.

4. Introduction

4.1. Background

While surgical resection remains the gold standard for the treatment of localized well-defined lung tumors, many patients are medically inoperable due to existing comorbidities. For this reason, alternative modalities are needed as an option for inoperable subjects.

Image-guided thermal ablation is a minimally invasive option that is becoming increasingly accepted for solitary lung tumors or selected metastatic tumors in patients who are medically inoperable.[3] Approaches include radiofrequency ablation, microwave ablation, cryoablation, and laser ablation.[4, 5]

Radiofrequency ablation has been the most well-characterized thermal ablation method to date. Radiofrequency ablation uses electromagnetic energy to induce local tissue heating and cell death by coagulation necrosis.[6, 7] Radiofrequency ablation has been recommended for peripheral tumors < 3 cm in inoperable patients.[8] While effective, use of radiofrequency ablation is limited by high rates of incomplete ablation and local recurrence, particularly in large tumors.[9, 10]

Microwave ablation involves placement and activation of an antenna directly into the target tissue. The system generates an alternating electric field which radiates microwave energy into target tissue. This causes rotation of water molecules, leading to friction, and resulting in thermal necrosis of the tissue. Advantages of microwave ablation over radiofrequency ablation include faster treatment of a larger tissue volume, and the minimization of the heat sink effect, in which local recurrence is increased in perivascular regions when heat is drawn away from the ablation zone by flowing blood faster than can be generated by the ablation device. Faster, hotter, and larger ablation zones also reduce the number of antenna placements required.[4, 5, 11]

However, previously available microwave ablation systems were still challenged by variations in the anatomical environment (e.g., proximity to large vessels, size of tumor, tissue type, tissue hydration), particularly in the lung. These factors influence the predictability of ablation zone size and shape, preventing complete ablation of diseased tissue and ultimately resulting in local recurrence.

The Emprint™ Ablation Catheter Kit with Thermosphere™ Technology is a novel thermal ablation device that uses wavelength-controlled, field-based energy to deliver adequate energy to create a large, spherical active zone regardless of tissue environment.[12-14] This resilience to anatomical distortion minimizes reliance on passive heating and reduces the number of overlapping ablations required to achieve a desired ablative effect.

The safety and performance data currently available for use of the Emprint™ Ablation System in the lung include a published study[15] and an unpublished sponsored study (Clinicaltrials.gov identifier NCT02323854) describing use of the Emprint™ Ablation System using a percutaneous approach. These studies demonstrate that the Emprint™ Ablation System performed as expected in the lung with a safety

profile consistent with the known safety profile for ablation in the lung. Additionally, an external research project has been initiated which will report on a retrospective analysis of use of the Emprint™ Ablation System in lung malignancies using a percutaneous approach.

The safety of image-guided bronchoscopic access of lung nodules using the superDimension™ navigation system has been established. In a meta-analysis of 15 published studies, pneumothorax occurred in 3.1% of patients (1.6% with intervention) and minor/moderate bleeding in 0.9%.[16] This is lower than the pooled complication rates of computed tomography (CT)-guided transthoracic core biopsy and fine-needle aspiration across 32 publications: 18.8%-25.3% pneumothorax, 4.3%-5.6% pneumothorax with intervention, 6.4%-18.0% pulmonary hemorrhage, and 1.7%-4.1% hemoptysis.[17]

The Emprint™ Ablation Catheter with Thermosphere™ Technology was introduced as part of the Emprint™ Ablation System to provide a bronchoscopic approach using the superDimension™ navigation system. The current clinical study will be conducted to characterize the safety and performance of the Emprint™ Ablation Catheter with Thermosphere™ Technology for bronchoscopic thermal ablation in the lung.

4.2. Purpose

The purpose of this investigation is to characterize the safety and performance of the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology in clinical use.

5. Objectives and Endpoints

5.1. Objectives

5.1.1. Primary Objective

The primary objective of this prospective, single-arm, multicenter, non-randomized study is to characterize the safety of the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology device in subjects undergoing lung ablation procedures.

The primary endpoint is the composite rate of adverse events (AEs) related to the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology through 1-month follow-up.

5.1.2. Secondary Objectives

The following secondary endpoints will be evaluated:

- Composite rate of serious AEs (SAEs) related to the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology through 1-month follow-up.
- Composite rate of all AEs related to the procedure or study devices through 1-month follow-up.

- Composite rate of all SAEs related to the procedure or study devices through 1-month follow-up.
- Patient satisfaction and pain (Bronchoscopic Ablation Patient Pain and Satisfaction Survey)
- Quality of life evaluation (EQ-5D scale)
- Technical success: An evaluation of whether the lung nodule was treated according to the study protocol as determined at the immediate post-procedural timepoint. This is in contrast to procedures in which the protocol could not be executed completely, either for technical reasons or for reasons related to comorbid disease.[2]
- Technique efficacy: An evaluation of whether the lung nodule was effectively ablated. Evaluates whether complete ablation of the nodule was achieved as evidenced by imaging follow-up 1-month post-procedure (including a window of 20-40 days post-procedure).[2]

6. Study Design

This is a prospective, single-arm, multicenter, non-randomized study. Up to 3 sites in up to 3 countries/regions will enroll up to 30 subjects in total. The study is designed to characterize the safety and performance of the bronchoscopic ablation procedure using the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology.

6.1. Duration

Assessments will occur at baseline, during and immediately post-procedure, and at 1-month follow-up.

The expected duration of each subject's participation in the study from the baseline visit to the 1-month follow-up is up to approximately 2 months (based on a baseline visit a maximum of 30 days pre-procedure and a follow-up window up to 40 days post-procedure).

Based on the expected enrollment rate of 1 subject per site per month, the total duration of the study from first subject enrollment to last subject follow-up is expected to be approximately 18 months.

6.2. Rationale

This study is a prospective, single-arm, multicenter, non-randomized study. Up to 3 sites in up to 3 countries will enroll up to 30 subjects in total. The study is designed to characterize the safety and performance of the bronchoscopic ablation procedure using the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology.

This study is single-arm and is not statistically powered. A maximum number of sites and subjects is proposed in order to provide a multicenter evaluation while minimizing risk to subjects. Enrollment of subjects who are not candidates for lung surgical resection or SBRT (or who refuse surgical resection or SBRT) will minimize exposure to only those with limited clinically viable options. Restricting nodules to those with ≥5mm of nodule-free lung parenchyma between the target nodule and pleura or fissure and excluding target nodules abutting the main stem bronchus, main pulmonary vasculature, esophagus

and/or trachea will minimize exposure and risk to the vasculature and surrounding tissue. While these inclusion/exclusion criteria are designed to minimize risk to subjects, results may not be generalizable to other populations of patients not evaluated as part of this study protocol. In addition, the results of this study will represent the outcomes in a small number of centers with experienced users and may not be generalizable across all institutions. If the study results support further clinical research, additional studies will examine a broader patient population across more diverse clinical sites.

Prior bench, preclinical, and clinical testing to justify the current clinical evaluation of the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology have been described in the Clinical Evaluation Report for the Covidien Emprint™ Ablation System and Accessories and are summarized briefly below.

Design verification and validation test results provide reasonable assurance that the device conforms to the requirements for its indications for use and intended use.

Extensive bench verification was performed to confirm the catheter's compatibility with the system generator, demonstrate its robustness to mechanical stresses, and establish its reliability, after conditions of misuse. Tissue-based testing was conducted using an ex-vivo soft tissue model (bovine liver) to confirm functionality. The catheter passed all verification tests, meeting all of the associated design requirements. The verification tests were designed to be clinically relevant and their successful completion supports the readiness of the device for clinical use. All reported deviations were minor in nature and did not impact the overall test result.

Biocompatibility evaluations and appropriate testing were performed on the patient contact components of the Emprint™ Ablation System. Arnitel EM740 (Trans Grey 431 C) is the only patient-contacting material in the ablation catheter (all other materials are considered non-patient contacting). The catheter passed all ISO and MHLW cytotoxicity, sensitization, and hemolysis tests as well as ISO systemic injection testing, ISO intracutaneous testing, and physiochemical testing.

A Covidien-sponsored chronic in vivo study examined use of the Emprint™ Ablation Catheter in 6 domestic male swine undergoing lung bronchoscopic ablation in a survival study. All ablations were performed using the Emprint™ Ablation Catheter with the Emprint™ Ablation System. Safety endpoints included incidence/severity assessment of pneumothorax, intra-operative bleeding assessment after device use, macroscopic/microscopic evaluation of representative tissues, and overall animal health. Observations did not raise a safety concern regarding use of the ablation catheter or microwave ablation procedure in the lung and were consistent with known clinical findings in humans. Most findings were considered common observations in laboratory animals following an anesthetic and surgical procedure and no abnormalities were attributed to the catheter device.

Eight published clinical studies evaluated the safety and performance of the Emprint™ ablation system for primary or metastatic cancer. Six studies were conducted in the liver,[18-23] 1 in the pancreas,[24] and 1 in the lung.[15] Ierardi 2017 evaluated 19 patients with 31 primary or metastatic lung tumors (28 microwave ablation procedures) undergoing percutaneous lung ablation with the Emprint™ ablation system.[15] Only

1 major complication occurred: pneumothorax. Minor complications included self-resolving pneumothorax (14 of 28 sessions) and perilesional hemorrhagic effusion (13 of 28 sessions), as well as hospitalization-related lower urinary tract infection in 3 of 28 sessions.[15] An additional unpublished sponsored study (NCT02323854) also describes use of the Emprint™ Ablation System in the lung using a percutaneous approach in 15 subjects. All 15 subjects underwent ablation followed by planned surgical resection. Complete ablation was detected in 54.4% (6/11), incomplete ablation in 36.4% (4/11), and delayed necrosis in 9.1% (1/11). There were no device-related AEs reported. A total of 5 SAEs occurred in 3 subjects (20%). SAEs included acute respiratory failure, pulmonary air leakage, prolonged air leak, Guillain-Barre Syndrome, and respiratory arrest, which resolved after the procedure. All 5 SAEs were either not related or unlikely to be related to the procedure. Twelve AEs were related to the ablation procedure, including bleeding, pneumothorax (Grade 1, n=4), hemoptysis (Grade 1, n=1), hemothorax (Grade 2, n=2), and vasovagal syncope (Grade 1, n=1). These studies demonstrate that the Emprint™ Ablation System performed as expected with a safety profile consistent with the known safety profile for lung ablation.

The Emprint™ Ablation Catheter was introduced as part of the Emprint™ Ablation System in 2016. Its CE mark was based on equivalence to the percutaneous antenna utilizing the same Thermosphere™ technology. Therefore, the proposed clinical study will be conducted specifically to characterize the safety and performance of the catheter device in the lung with a bronchoscopic approach.

7. Product Description

7.1. General

The device under study is the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology (CA108L1), an endoscopic ablation accessory for use with the Emprint™ Ablation System. The Emprint™ Ablation Catheter Kit with Thermosphere™ Technology is for use with the Emprint™ Ablation System with Thermosphere™ Technology for the ablation of lung tissue.

Microwave-based soft tissue ablation uses microwave energy to increase target tissue temperature resulting in thermocoagulation and cellular death. Microwave energy is supplied by a generator and emits from the exposed portion of an antenna. The Evident™ Microwave Ablation System was designed to provide microwave power for ablation of soft tissue during medical procedures. It received the CE mark in 2007 and 510k clearance in 2008. The Emprint™ Ablation System is an evolution of the technology within the Evident™ Microwave Ablation System, which received both CE mark and 510k clearance in 2014. The Emprint™ system utilizes higher power, a more efficient cable and antenna design, and an antenna designed to create a more spherical field pattern (Thermosphere™ technology). An ablation catheter has been added as an accessory to the Emprint™ system- to be used in a bronchoscopic approach for lung ablation.

The shelf life of the product is intended to be expanded to 24 months which may occur during the course of the study. No other changes to the product are anticipated.

7.2. Dosage Form and Route of Administration

The Emprint™ Ablation Catheter Kit with Thermosphere™ Technology is deployed endoscopically (bronchoscopically) and will be used to conduct bronchoscopic ablations in the lung using the superDimension™ navigation system.

7.3. Manufacturer

The Emprint™ Ablation Catheter Kit with Thermosphere™ Technology is manufactured by Covidien llc, an indirect wholly owned subsidiary of Medtronic plc.

7.4. Packaging

The Emprint™ Ablation Catheter will be provided to health care providers as part of a kit (Catalog No. CA108L1). In addition to the catheter, the kit includes a stabilizing rail that is attached to the Edge Bronchoscope Adapter and a locking clip. Products used in this study that are commercially available are packaged and labelled accordingly. Labeling of devices will be provided in accordance with local language requirements.

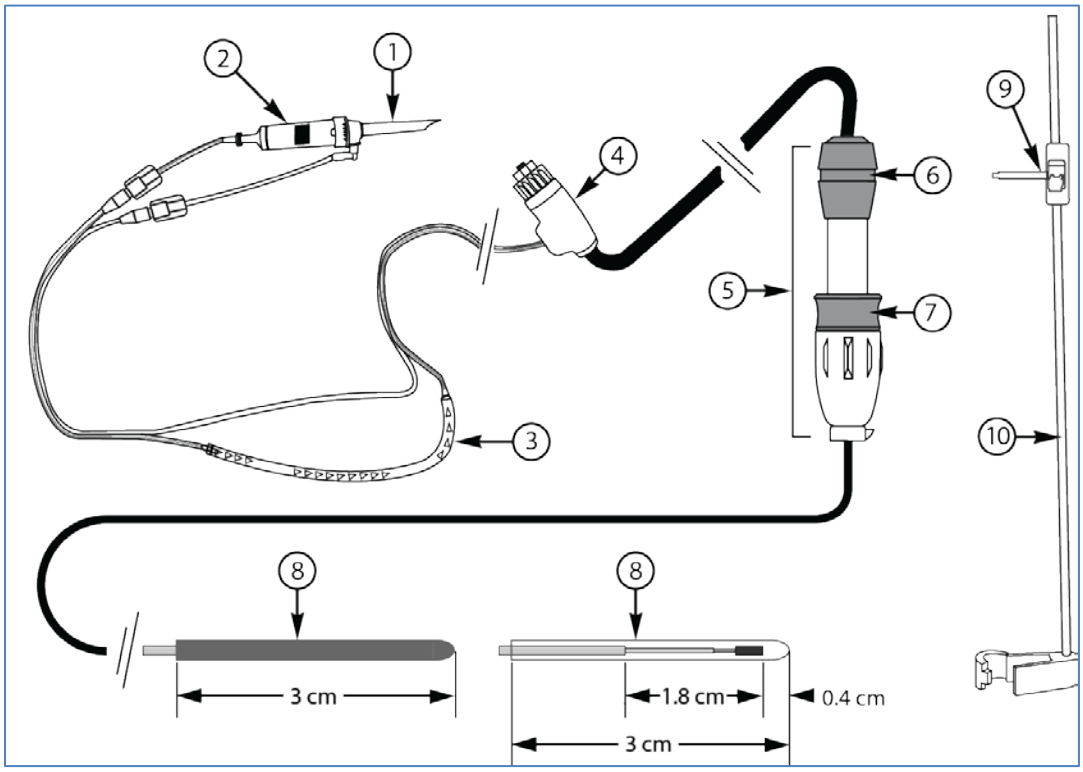


Figure 1. The Emprint™ Ablation Catheter, rail, and clip. (1) Intravenous IV Bag Spike; (2) Drip Chamber; (3) Pump Tubing; (4) Generator Connector; (5) Ablation Catheter Handle; (6) Top Groove, (7) Control Ring, (8) Radiating Section; (9) Clip; (10) Rail

7.5. Intended Use and Population

The Emprint™ Ablation System with Thermosphere™ Technology is intended for use in percutaneous, laparoscopic, endoscopic, and intraoperative coagulation (ablation) of soft tissue, including partial or complete ablation of non-resectable liver tumors.

The Emprint™ Ablation System with Thermosphere™ Technology is not intended for use in cardiac procedures.

This study will evaluate the population of patients where the use of the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology is conducted via a bronchoscope for ablation of malignant nodules in the lung.

7.6. Equipment

The Emprint™ Ablation Catheter is designed for use with the Emprint™ system components (Figure 1 above) and is compatible with the Covidien Edge™ or Edge™ Firm Tip Extended Working Channel (EWC)

and Edge Bronchoscope Adapter. The system's reusable cable (connects the percutaneous antenna to the microwave generator) is not used with the flexible catheter, as the catheter is designed to connect to the generator directly.

Sites must have access to the superDimension™ navigation system utilizing either software version 6 or higher at the time of study initiation for each site, with potential for upgrade to the most recent software release throughout the duration of the study. Sites must also have a procedure room equipped with a cone-beam computed tomography (CBCT) imaging system. Sites may also use the CrossCountry™ Transbronchial Access Tool to obtain access.

7.7. Product Use

For the purpose of this post-market clinical study, the Emprint™ ablation catheter and Emprint™ Ablation Catheter Kit with Thermosphere™ Technology should be used according to manufacturer's Instructions for Use and standard-of-care. Typically, one ablation catheter is used per procedure but more than one may be used at the investigator's discretion.

7.8. Product Training Requirements

Physicians must have documented completion of the manufacturer's bronchoscopic ablation training program and sufficient experience conducting ENB procedures and in using CBCT, the CrossCountry™ Access Tool, and the Emprint™ ablation system. Documented completion will be recorded on the Study Enrollment Eligibility Form.

7.9. Product Receipt, Tracking, Storage, Return, and Accountability

The study devices provided by the Sponsor will be recorded on the study specific Product Accountability Log. Information to be recorded will include, but is not limited to, date of receipt, and the date used or date of return to the Sponsor. The study-specific devices shall be kept in a locked room.

The study devices provided by the Sponsor will be labeled with a study-specific label indicating that it is only to be used for study subjects.

7.10. Intended Claims

The purpose of this investigation is to characterize the safety and performance of the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology in clinical use. This study does not specifically evaluate efficacy claims.

8. Selection of Subjects

8.1. Study Population

The study population will consist of consented adults undergoing bronchoscopic lung ablation procedures using electromagnetic navigation bronchoscopy (ENB). Additional inclusion and exclusion criteria are listed below.

8.2. Subject Enrollment

Up to 30 subjects will be enrolled at up to 3 sites in up to 3 regions. The minimum and maximum number of subjects to be included at each site are not prespecified since the study is not statistically powered.

For the purpose of this clinical study investigational plan, the point of enrollment is defined as the insertion of the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology into the EWC.

Subjects will be approached to obtain written informed consent prior to any institution non-standard-of-care assessments or study-specific data being collected. During the index procedure imaging, nodule eligibility criteria will be re-confirmed. Any patients with nodules no longer meeting eligibility criteria will not be enrolled. Subjects who provide study consent but then are determined to be ineligible prior to the insertion of the ablation catheter will be considered screen failures and documented as such in the database.

8.3. Inclusion Criteria

1. Subject is ≥ 18 years of age
2. Subject has provided informed consent
3. Subject is able and willing to comply with the study follow-up schedule
4. Subject has a definitive diagnosis of cancer in the lung
5. Target nodule is ≤ 30mm in maximum diameter
6. There is ≥ 5mm of nodule-free lung parenchyma between target nodule and pleura or fissure
7. Subject is a candidate for an elective ENB procedure
8. Subject is a candidate for an elective lung ablation procedure according to standard of care and product Instructions for Use
9. Subject is not a candidate for lung surgery or refuses lung surgery
10. Subject is not a candidate for stereotactic body radiation therapy (SBRT) or refuses SBRT

8.4. Exclusion Criteria

1. Target nodule is abutting main stem bronchus, main pulmonary vasculature, esophagus and/or trachea
2. Patients currently diagnosed with Global Initiative for Chronic Obstructive Lung Disease (GOLD) Stage IV emphysema
3. Female subjects who are pregnant or nursing as determined by standard site practices
4. Subject has participated in an investigational drug or device research study within 30 days of enrollment that would interfere with this study
5. The investigator determines that participation in the study may jeopardize the safety or welfare of the subject

9. Study Procedures

Following confirmation of eligibility and informed consent, subjects with inoperable lung nodules will undergo an ablation procedure using a bronchoscopic approach. A target nodule will be identified on a pre-procedure CBCT scan. Nodule localization will be aided by ENB using the superDimension™ navigation system. Once localized, if no suitable bronchus sign leads to the proposed area to ablate, access to the region may be obtained using the CrossCountry™ Transbronchial Access Tool. Once ablation region access has been achieved, the ablation catheter will be placed inside the EWC and will be unsheathed inside the target nodule. Correct positioning will be verified using CBCT and the nodule will then be ablated. AEs related to Emprint™ Ablation Catheter Kit with Thermosphere™ Technology, accessory devices, or study procedures will be captured and reported until the 1-month follow-up visit.

9.1. Schedule of Events

Variables to be collected (following confirmation of eligibility and written informed consent), follow-up visit schedule, and tests to be performed at each visit are described in **Table 1** below.

Table 1. Schedule of Events.

	Baseline (Day -30 to Day 0)	During the Procedure and Immediately Post-Procedure	1-Month Follow-up (20 to 40 Days Post-Procedure)
Subject demographics	X		
Medical history (Lung Diagnoses, Previous Lung procedures, Lung function tests, etc.)	X		
Eligibility assessment	X	X	
Nodule characteristics		X	
Procedural information		X	
Adverse event assessment		X	X
Imaging	X*	X	X
Concomitant medications	X	X	X
Quality of life survey (EQ-5D)	X		X
Bronchoscopic Ablation Patient Pain and Satisfaction Survey			X

*Standard-of-care CT scan performed prior to consent.

9.2. Subject Screening

A baseline visit will be performed within 30 days prior to the scheduled procedure to assess study eligibility. During the index procedure imaging, nodule eligibility criteria will be re-confirmed. Consented subjects will be considered for the study if they meet specified inclusion criteria and none of the exclusion criteria. The criteria for enrollment must be followed explicitly.

Subjects who provide study consent, but then are determined to be ineligible prior to the start of the ablation portion of the procedure will be considered screen failures and will not require additional study follow-up visits. The reason for the Screen Failure will be clearly documented on the applicable electronic case report forms (eCRFs). Screen failures will not be counted towards the number of study subjects.

9.3. Prior and Concomitant Medications

All prior and concomitant medications should be managed according to standard-of-care.

9.4. Subject Consent

Subjects will be approached to obtain written informed consent prior to any institution non-standard-of-care assessments or study-specific data being collected. The purpose of the study and the benefits and risks of participating in the study will be explained to the subject and the consent process must be documented accordingly.

Subjects will be informed that their participation in this study is voluntary and that they may refuse to participate or discontinue from the study at any time. Additionally, subjects will be informed that despite signing informed consent, the screening assessments may demonstrate the subject is not a suitable candidate for the study or the ablation procedure and may be withdrawn. Subjects will be given the opportunity to ask the investigator questions so that they are adequately informed about the research.

After being informed of the nature of the study, subjects who agree to study participation must sign a written informed consent form (ICF) that has been approved by the appropriate Ethics Committee (EC) or Institutional Review Board (IRB) and Regulatory Authority if required per country, of the respective clinical site. A copy of the signed ICF must be provided to the subject.

For this study, the subject must sign and date the ICF personally. The use of Legally Authorized Representatives, Healthcare Proxies or any other means of representation will not be permitted. All procedures evaluated in this study are considered elective; no emergency procedures or circumstances where the subject is unable to give consent will be permitted according to the study inclusion criteria.

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.

The principal investigator or his/her authorized designee must conduct the informed consent process.

9.5. Randomization and Treatment Assignment

Not applicable. There are no treatment arms or randomizations required for this study.

9.6. Medication Compliance

Not applicable. There are no required medications or medication protocols for this study.

9.7. Assessment of Efficacy

The following efficacy endpoints will be evaluated:

- Technical Success: An evaluation of whether the lung nodule was treated according to the study protocol as determined at the immediate post-procedural timepoint. This is in contrast to procedures in which the protocol could not be executed completely, either for technical reasons or for reasons related to comorbid disease.[2]
- Technique Efficacy: An evaluation of whether the lung nodule was effectively ablated. Evaluates whether complete ablation of the nodule was achieved as evidenced by imaging follow-up 1-month post-procedure (including a window of 20-40 days post-procedure).[2]

Full procedures for study visits and the index ablation procedure are described in the section "Assessment of Safety" below.

9.8. Assessment of Safety

9.8.1. Screening / Baseline Visit

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

- Verification of eligibility criteria
- Subject demographics (e.g.,. subject age, sex, ethnicity, race)
- Subject medical history (e.g., COPD, asthma, emphysema, tobacco history, cancer diagnosis)
- History of prior invasive lung procedures
- Medication use (e.g., immunotherapy, chemotherapy, targeted antineoplastic therapy, prescription antithrombotics)
- Pulmonary function testing (if available per standard of care)
- Quality of Life Survey (EQ-5D)

9.8.2. Baseline Imaging

In accordance with inclusion criteria, nodules ≤ 30mm in maximum diameter with ≥ 5mm of nodule-free lung parenchyma between target nodule and pleura or fissure are eligible to be considered target nodules for the study analysis. This will be based on standard-of-care (SOC) baseline imaging.

One target nodule per subject will be identified on a SOC baseline CT prior to patient consent. If the study subject has more than one nodule meeting the above criteria, the most easily accessible nodule, as determined by the physician investigator, will be targeted for the study.

9.8.3. Nodule Characteristics

Nodule characteristics (e.g., size, location, morphology) will be captured at procedure.

9.8.4. Index Procedure

The index procedure workflow is shown in Figure 2. The EWC will be inserted and navigation to the target will be conducted according to the manufacturer's Instructions for Use.

CBCT will be used to confirm target nodule localization using fluoroscopy overlay. If CT indicates the absence of a bronchus sign leading to the center of the target nodule, access to the nodule may be obtained using the CrossCountry™ Transbronchial Access Tool under CBCT guidance.

During the index procedure imaging, nodule eligibility criteria will be re-confirmed. Any patients with nodules no longer meeting eligibility criteria will not be enrolled. For the purpose of this clinical study investigational plan, the point of enrollment is defined as the insertion of the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology into the EWC.

A high-level procedure workflow is shown below. Investigators will refer to the manufacturer's instructional documents for additional detail.

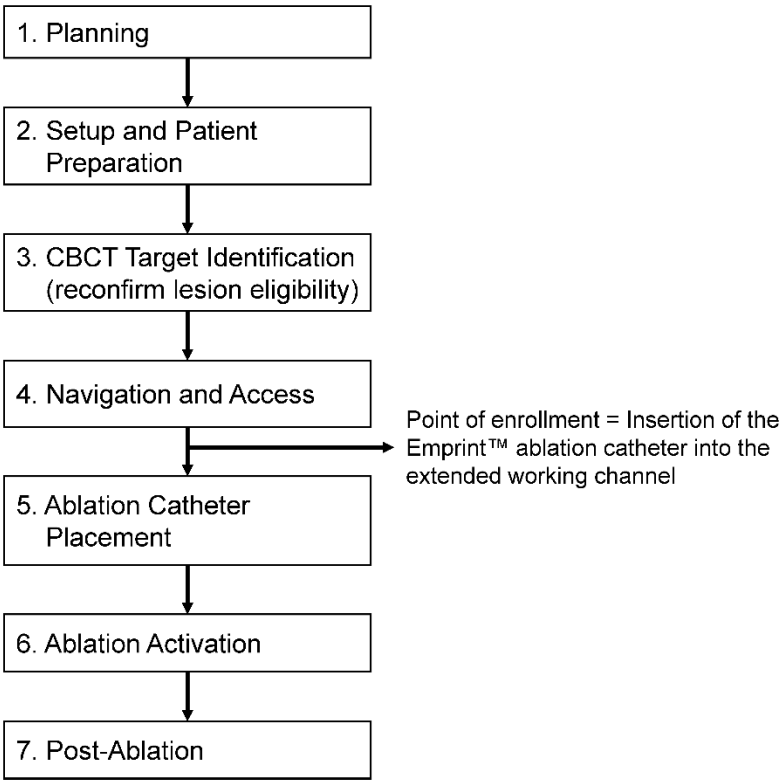


Figure 2. Index procedure workflow

9.8.5. Safety Endpoints

The primary objective of this prospective, single-arm, multicenter, non-randomized study is to characterize the safety of the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology device in subjects undergoing lung ablation procedures.

The primary endpoint is the composite rate of AEs related to the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology through 1-month follow-up.

In addition, the following secondary safety endpoints will be evaluated:

- Composite rate of SAEs related to the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology through 1-month follow-up.
- Composite rate of all AEs related to the procedure or study devices through 1-month follow-up.
- Composite rate of all SAEs related to the procedure or study devices through 1-month follow-up.

All AEs related to the Emprint™ Ablation Catheter with Thermosphere™ Technology will be graded for severity based on the Common Terminology Criteria for Adverse Events.[1]

For safety reporting, only AEs related to the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology, accessory devices, or study procedures will be captured and reported until the subject exits the study (refer to Section 11.1 for additional details). Related AEs will be summarized as the event counts and percentage which occurred during the ablation procedure or detected after the procedure within the 1-month reporting timeframe. For the primary endpoint, relationship specifically to the Emprint™ Ablation Catheter with Thermosphere™ Technology device will be assessed.

9.8.6. 1-Month Follow-Up

The study subject will complete the study at the conclusion of the 1-month follow-up visit, conducted per standard local practice, but within the window of 20-40 days after the study index procedure.

The following assessments will be performed and the results recorded on the appropriate subject eCRFs:

- Medication use (e.g., immunotherapy, chemotherapy, targeted antineoplastic therapy, prescription antithrombotics)
- A follow-up CT scan at this timepoint will be used for the evaluation of Technique Efficacy
- AE assessment (AEs related to the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology, accessory devices, or study procedures)
- Quality of life survey (EQ-5D)
- Bronchoscopic Ablation Patient Pain and Satisfaction Survey

9.8.7. Study Completion

Subjects will complete the study at the completion of the 1-month post-procedure visit. No additional study-specific care will be provided to study subjects after completion of the study. Standard of care should continue. The reporting window for the 1-month follow-up is 20-40 days.

9.9. Recording Data

This study will utilize an eCRF. The eCRF will be used to capture the required data elements. Medical and study records, rather than eCRFs, will serve as the source documentation.

9.10. Deviation Handling

No written waivers from the CIP will be granted. The Principal Investigator must make every effort to follow the CIP, unless the deviation is necessary in an emergent situation to protect the rights, safety and/or well-being of the subject. Deviations from the CIP will be collected on a Protocol Deviation CRF and reviewed with the Principal Investigator to ensure compliance.

The investigator must notify Medtronic and the reviewing ethics committee (EC) / institutional review board (IRB) 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 five (5) working days after the emergency has occurred. All study deviations will be reported by Medtronic to the Regulatory Authority (if applicable) via either Final Clinical Study Report or separate notification in case of substantial CIP deviation, for which the Regulatory Authority approval is required before its implementation.

If a pattern of non-compliance is noted, the study manager will determine the course of action to take, such as root cause, review relevant CIP procedures and as applicable retrain and verify understanding of the issue in question. This will be documented in the Study Master Files. In the case of repeated or serious non-compliance, the Sponsor reserves the right to disqualify the offending site.

9.11. Subject Withdrawal or Discontinuation

Subjects may voluntarily withdraw from the study if they no longer wish to have their study-related information used. Additionally, the Principal Investigators may withdraw or choose not to enroll subjects if they feel they do not meet the CIP defined inclusion and exclusion criteria or if it is in the best medical interest of the subjects in question.

In cases of voluntary subject withdrawal, all data collected from the time of informed consent to the time of voluntary withdrawal may be used. The General Data Protection Regulation (GDPR) process will be followed as applicable per country regulations. Withdrawn subjects will not be replaced. Enrollment will continue as per CIP definitions up to the predefined maximum number of subjects.

All subjects will be followed per institutional standard of care after any withdrawal, discontinuation, or completion of the study follow-ups.

The reason for study exit of all enrolled subjects will be documented on the applicable electronic case report form (eCRF). In the event the subject withdraws consent during the study, the date of withdrawal will be documented. If the study investigator voluntarily removes a subject from further study participation, supporting documentation must be in place for the rationale and date of removal. Every attempt will be made to contact subjects who are noncompliant. Subjects will be considered lost to follow-up once the following steps have been taken:

- Three phone calls should be made to the subject. Each attempt should be clearly documented in the source documents and the response or lack thereof should be captured.
- If there is no response to the phone calls, then a certified/registered letter should be written to the subject. A copy of the letter should be retained in the subject's source document.
- After a period of one week following completion of the above actions, the subject will be considered lost to follow-up. The sponsor should be notified and the Study Exit form should be completed.

10. Risks and Benefits

10.1. Potential Risks

The potential risks of the Emprint™ Ablation System have been described in the Risk Management Report for the Emprint Ablation System with Ablation Catheter and the Clinical Evaluation Report for the Covidien Emprint™ Ablation System and Accessories and are summarized briefly below. The clinical investigation has been designed to involve as little pain, discomfort, fear, and any other foreseeable risk as possible for the subjects, and both the risk threshold. The degree of distress are specifically defined in the clinical investigation plan and constantly monitored.

10.1.1. Summary of Risk Management Report

A clinical risk/benefit analysis evaluated whether the Emprint™ Ablation System with Ablation Catheter is likely to provide more benefit than harm. Listed below are the high-risk residual risks from the risk analysis. All of the residual risks listed below have been described in the literature as known and/or experienced complications of ablation procedures. All patients who undergo an ablation procedure are consented for such risks. Benefit estimation describes the expected performance of the device, expected clinical outcome, and risks and benefits related to other procedural options. The risk/benefit comparison documents the judgments of whether the benefits exceed the residual risks.

- Pleural effusion
- Intraparenchymal pulmonary hemorrhage / bronchopulmonary hemorrhage
- Pain/shoulder pain
- Mortality
- Pyothorax
- Atrial fibrillation
- Hemolysis
- Pulmonary/upper respiratory fistula
- Hemothorax
- Abscess
- Hematoma
- Hemoptysis
- Pneumonia
- Pulmonary edema
- Ventricular arrhythmia
- Unintended microwave burn – unintended tissue ablation
- Unintended microwave burn – vessel thrombosis /thrombus /embolism

- Unintended microwave burn – diaphragmatic paresis

Expected AE rates are described in Section 10.1.2 below.

In accordance with the safety assessments described in Section 9.8.5, risks will be continuously monitored, assessed and documented by the investigator.

10.1.2. Summary of Clinical Evaluation Report

A Clinical Evaluation Report (CER) for the Covidien Emprint™ Ablation System and Accessories was performed according to the provisions of the Medical Devices Directive 93/42/EEC (MDD), as amended by Directive 2007/47/EC. This report was prepared in accordance with the following Guidelines and Standard Operating Procedures (SOPs) to provide evidence of the medical safety and performance of the Emprint™ Ablation System and Accessories for its intended use: MEDDEV 2.7/1 rev. 4 (June 2016), MEDDEV 2.12/2 rev. 2 (January 2012). The intent of this CER was to provide evidence that the Emprint™ Ablation System and Accessories are safe, effective, and state-of-the-art for the indications and intended use, through a critical review of product-related documents, testing, published clinical literature and post-market data. A brief summary of that report is included below.

The safety of the Emprint™ Ablation System has been assessed in 8 clinical studies evaluating its use in the liver,[18-23] pancreas,[24] and lung,[15] as well as complaints and vigilance reports of 27,150 devices sold. All complications occurred in < 1% of patients each (total complication rate 4.7%). This is comparable to or better than the 10.3% complication rate in the liver for minor and major complications reported in the literature. The majority of complications reported with use of microwave ablation in the lung (such as pneumothorax and hemorrhagic effusion) were from one clinical publication and one clinical investigation and are either known complications of microwave ablation or were deemed to not be related to the device or the procedure. In one clinical publication of microwave ablation in the pancreas, pain was the only complication reported. Pain is a common complication, and often resolves spontaneously or with treatment.

In the post-market complaints and vigilances report spanning a 5-year period, all confirmed injuries are known to occur with microwave ablation. In addition, 5 of 7 deaths reported occurred in patients with major comorbidities.

All complications that occurred with use of the Emprint™ MWA ablation system in the liver, lung, and pancreas are either known to occur with microwave ablation or were deemed to be unrelated. In addition, complications in the liver and lung occurred at similar rates to other microwave ablation devices reported in the literature.

10.1.3. Radiation Exposure

There are risks associated with the use of x-ray fluoroscopy, CBCT, and CT imaging for this study.

The CT scan and the imaging that will be carried out as part of the ablation procedure are part of the patient's routine care. These procedures use ionizing radiation to form images of the body and provide the doctor with other clinical information. Ionizing radiation can cause cell damage that may, after many years or decades, turn cancerous. The chances of this happening are the same whether patients take part in this study or not. It should be noted that radiation dose will vary based on the type of imaging system used and the size of the patient.

10.2. Potential Benefits

Benefit estimations of the general use of the Emprint™ Ablation Catheter with Thermosphere™ Technology are described in the Risk Management Report for the Emprint™ Ablation System with the Ablation Catheter.

Microwave ablation is an alternative for patients with lung cancer who are either ineligible for or refuse other treatments such as surgical resection. Furthermore, bronchoscopic ablation may result in fewer complications than percutaneous ablation (see Section 4.1). For patients who are not candidates for alternative therapies, the benefits of microwave ablation outweigh the risks described above.

The bronchoscopic ablation procedure described in this study is commercially available. Patients could receive these potential benefits without taking part in the study and may not gain any direct medical benefits compared to routine care. However, the data collected from this study will help characterize the safety and performance of the Emprint™ Ablation Catheter with Thermosphere™ Technology. If the results of this study support additional clinical research, further studies may be justified to evaluate the potential for improved standard-of-care using microwave ablation technology in lung nodules.

10.3. Risk-Benefit Rationale

As described in the Risk Management Report for the Emprint™ Ablation System with the Ablation Catheter, performing image-guided microwave ablation involves risk. Complications have been reported in the literature associated with thermal ablation of the lung. These complications are associated with both the intervention itself and patient comorbidity. For patients who are not candidates for alternative therapies, the benefits of microwave ablation described above outweigh these risks.

11. Adverse Events and Device Deficiencies

11.1. Definitions/Classifications

Adverse event (AE) definitions used in this study are based on ISO 14155:2011 (Clinical Investigation of Medical Devices for Human Subjects -- Good Clinical Practice; https://www.iso.org/obp/ui/#iso:std:iso:14155:ed-2:v1:en), which is aligned with MEDDEV 2.7/3

Revision 3, May 2015 (Guidelines on Medical Devices, Clinical Investigations: Serious Adverse Event Reporting).

For the purpose of this clinical study investigational plan, the point of enrollment is defined as the insertion of the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology into the EWC. AEs will be collected beginning at the point of enrollment. For safety reporting, only AEs related to the procedure or study devices will be captured and reported until the subject exits the study. Any unresolved procedural or device related events that are still ongoing past study exit will be monitored by the physician per their institutional standard-of-care.

Anticipated AEs are listed in Section 10.1.

AEs related to the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology, accessory devices, or study procedures will be adjudicated by an independent medical monitor.

Refer to the NAVABLATE Adverse Event Reference List (Appendix 17.5) for additional definitions.

11.1.1. Adverse Event (AE)

An AE 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 investigational medical device.*

*For the purposes of this clinical study, AE definitions will be ISO 14155:2011 compliant with the following exception: only those AEs that are related to the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology, accessory devices, or study procedures will be captured and reported.

NOTE 1: This definition includes events related to the investigational medical device or the comparator.

NOTE 2: This definition includes events related to the procedures involved.

NOTE 3: For users or other persons, this definition is restricted to events related to investigational medical devices.

11.1.2. Serious Adverse Event (SAE)

For the purposes of this study, a Serious Adverse Event (SAE)* is an AE that has

1. Led to death,
2. Led to serious deterioration in the health of the subject, that either resulted in
    a. A life-threatening illness or injury, or
    b. A permanent impairment of a body structure or a body function, or
    c. In-patient or prolonged hospitalization, or
    d. Medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function.

3. Led to foetal distress, foetal death or a congenital abnormality or birth defect

NOTE 1: This includes device deficiencies that might have led to an SAE if a) suitable action had not been taken or b) intervention had not been made or c) if circumstances had been less fortunate. These are handled under the SAE reporting system.

NOTE 2: Planned hospitalization for a pre-existing condition, or a procedure required by the clinical investigational plan, without serious deterioration in health, is not considered an SAE.

*For the purposes of this clinical study, SAE definitions will be ISO 14155:2011 compliant with the following exception: only those SAEs that are related to the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology, accessory devices, or study procedures will be captured and reported.

11.1.3. Adverse Device Effect (ADE)

An Adverse Device Effect (ADE) is an AE related to the use of the investigational medical device (the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology).

NOTE 1: This definition includes AEs resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device.

NOTE 2: This definition includes any event resulting from use error or from intentional misuse of the investigational medical device.

11.1.4. Serious Adverse Device Effect (SADE)

A Serious Adverse Device Effect (SADE) is an adverse device effect that has resulted in any of the consequences characteristic of an SAE.

11.1.5. Unanticipated Serious Adverse Device Effect (USADE)

An Unanticipated Serious Adverse Device Effect (USADE) is defined as serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current version of the Risk Management Report.

NOTE: Anticipated serious adverse device effect (ASADE) is an effect which by its nature, incidence, severity or outcome has been identified in the risk analysis report.

11.1.6. Device Deficiency

Inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance.

Note: Device deficiencies include malfunctions, use errors, and inadequate labelling.

11.1.7. Adverse Event Relationship Classification

Causality assessments define the relationship between the use of the medical device (including the procedure) and the occurrence of each AE. During causality assessment activity, clinical judgment shall be used and the relevant documents, such as the MDR Reportable Event Trend & Risk Analysis Report shall be consulted, as all the foreseeable SAEs and the potential risks are listed and assessed there. The presence of confounding factors, such as concomitant medication/treatment, the natural history of the underlying disease, other concurrent illness or risk factors shall also be considered.

Each AE and SAE will be classified according to five different levels of causality. The following definitions will be used to assess the relationship of the AE to the investigational medical device (the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology), accessory devices, or study procedures:

- *Not related*: Relationship to the device or procedures can be excluded when:
  - the event is not a known side effect of the product category the device belongs to or of similar devices and procedures
  - the event has no temporal relationship with the use of the investigational device or the procedures;
  - the serious event does not follow a known response pattern to the medical device (if the response pattern is previously known) and is biologically implausible;
  - the discontinuation of medical device application or the reduction of the level of activation/exposure - when clinically feasible – and reintroduction of its use (or increase of the level of activation/exposure), do not impact on the serious event;
  - the event involves a body-site or an organ not expected to be affected by the device or procedure;
  - the serious 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);
  - the event does not depend on a false result given by the investigational device used for diagnosis, when applicable;
  - harms to the subject are not clearly due to use error;
  - In order to establish the non-relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the serious event.
- *Unlikely*: The relationship with the use of the device seems not relevant and/or the event can be reasonably explained by another cause, but additional information may be obtained.
- *Possible*: The relationship with the use of the investigational device is weak but cannot be ruled out completely. Alternative causes are also possible (e.g. an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or treatment). Cases were relatedness cannot be assessed or no information has been obtained should also be classified as possible.
- *Probable*: The relationship with the use of the investigational device seems relevant and/or the event cannot reasonably be explained by another cause, but additional information may be obtained.

- *Causal relationship*: The serious event is associated with the investigational 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 devices and procedures;
  - the event has a temporal relationship with investigational device use/application or procedures;
  - the event involves a body-site or organ that
  - the investigational device or procedures are applied to;
  - the investigational device or procedures have an effect on;
  - the serious 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 serious event (when clinically feasible);
  - other possible causes (e.g. an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or treatment) have been adequately ruled out;
  - harm to the subject is due to error in use;
  - the event depends on a false result given by the investigational device used for diagnosis, when applicable;
- In order to establish the relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the serious event.

Events will be distinguished between the SAEs related to the device and those related to the procedures (any procedure specific to the clinical investigation). An AE can be related both to procedures and the device. Complications of procedures are considered not related if the said procedures would have been applied to the patients also in the absence of device use/application.

In some particular cases the event may be not adequately assessed because information is insufficient or contradictory and/or the data cannot be verified or supplemented. The sponsor's Medical Monitor and the Investigators will make the maximum effort to define and categorize the event and avoid these situations. Where the Medical Monitor remains uncertain about classifying the serious event, it should not exclude the relatedness and classify the event as "possible".

11.1.8. Adverse Event Outcome Classification

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

- Fatal: If death was possibly, probably, or causally related to the event
- Not recovered / not resolved: Subject has exited the study and the AE is ongoing and not expected to resolve
- Recovered / resolved: The event has fully resolved prior to study exit

- Recovered / resolved with sequelae: The event has resolved prior to study exit, but retained pathological conditions resulting from the prior disease or injury
- Recovering / resolving: The subject has exited the study and the AE is ongoing but expected to resolve
- Unknown: The subject has exited the study and the AE outcome is unknown

11.2. Reporting of Adverse Events

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. AEs will be monitored until a subject completes the study. Any unresolved procedural- or device-related events that are still ongoing past study exit will be monitored by the physician per their institutional standard-of-care. AEs will be documented in the applicable source documentation and reported on an AE eCRF. To the extent possible, the event to be recorded and reported is the event diagnosis as opposed to event outcome (e.g. death) or symptoms (e.g., fever, chills, nausea and vomiting in the presence of a clinically diagnosed infection is to be reported as infection only).

The following should not be considered an AE:

- A condition requiring a preplanned procedure unless the condition worsened since enrollment
- A preexisting condition found as a result of screening, unless the condition has worsened since enrollment.

11.2.1. Notification to Authorities

The following events are generally considered reportable during the course of this study and should be reported within the timeframes outlined in **Table 2**:

- any AE or SAE related to the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology, accessory devices, or study procedures
- any Device Deficiency
- new findings/updates in relation to already reported events.

Table 2. Reporting of Adverse Events

Type	Report to	Reporting Timeframe (from time of learning of event)
Device Deficiency	Sponsor	Recommended within 10 working days
AE	Sponsor	Recommended within 10 working days
	EC/IRB	Per EC/IRB reporting requirements
SAE	Sponsor	Not to exceed 10 working days
	EC/IRB	Per EC/IRB reporting requirements

Events will be reviewed by sponsor or designee to determine any sponsor reporting obligations to Regulatory Authority and EC/IRB. All applicable events will be reported to Post-Market Vigilance (PMV) by sponsor clinical team; and PMV will also report to Regulatory Authorities when applicable.

AEs will be recorded on the **Adverse Event CRF.**

12. Data Review Committees

There will be no Data Monitoring Committee or Clinical Events Committee as these are not required for a post-market study of a commercially available product.

13. Statistical Design and Methods

All statistical analyses will be performed using Statistical Analysis System (SAS) for Windows (version 9.4 or higher, SAS Institute Inc. Cary, NC) or other widely accepted statistical or graphical software.

Descriptive statistics will be used to present the data and to summarize the results. Continuous variables will be summarized with number of subjects (n), mean, standard deviation, median, and ranges. Categorical variables will be summarized by frequencies and percentages.

The sample size of this study is not based on power calculations of a statistical hypothesis test.

There are no pre-planned interim or subgroup analyses. Any post-hoc subgroup analyses will be exploratory in nature for the purpose of evaluating the safety and performance of the study device under various clinical conditions.

Due to the post-market and observational nature of the study, no imputation is planned for missing data in the primary and secondary endpoints, if any. All available data from enrolled subjects will be reported.

A detailed Statistical Analysis Plan (SAP) will be prepared prior to data analysis.

Any deviations from this analysis plan will be documented in the final clinical study report.

14. Ethics

14.1. Statement(s) of Compliance

This clinical investigation will be conducted in accordance with this CIP, the ethical principles that have their origin in the Declaration of Helsinki, as well as with ISO 14155:2011 (Clinical Investigation of Medical Devices for Human Subjects – Good Clinical Practice), the European Union Medical Device Regulation, and the International Conference on Harmonisation (ICH) of Technical Requirements For Registration of Pharmaceuticals For Human Use, ICH Harmonised Tripartite Guideline for Good Clinical Practice E6 (R1). This investigation will also be conducted per applicable local regulatory requirements and laws in which the study will be conducted.

The study will be compliant with ISO 14155:2011 with the following exceptions:

- The point of enrollment is defined as the insertion of the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology into the EWC, rather than at the time of informed consent. Subjects will be approached to obtain written informed consent prior to any institution non-standard-of-care assessments or study specific data being collected. Subjects who provide study consent but then are determined to be ineligible prior to the insertion of the ablation catheter will be considered screen failures and documented as such in the database (see Section 8.2).
- For the purposes of this clinical study, AE definitions will be ISO 14155:2011 compliant with the following exception: only those AEs deemed to be related to the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology, accessory devices, or study procedures will be captured and reported (see Section 11.1.1).

The principles of the Declaration of Helsinki have all been implemented by means of the patient informed consent process, EC approval, study training, clinical study registration, preclinical testing, risk benefit assessment, and publication policy.

Pediatric, legally incompetent, or other vulnerable subjects are not eligible for the study.

The clinical investigation will not begin until all necessary approvals/favorable opinions are obtained from the appropriate EC/IRBs or Regulatory Authority, as appropriate. Should an EC/IRB 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 submitted for publication in an appropriate journal.

No insurance or compensation will be provided to study subjects.

Medtronic maintains appropriate clinical study liability insurance coverage as required under applicable laws and regulations and will comply with applicable local law and custom concerning specific insurance coverage. If required, a clinical study insurance statement/certificate will be provided to the EC/IRB.

15. Study Administration

15.1. Monitoring

Authorized Medtronic representatives will conduct site initiation visits prior to first subject enrolled at a site. Site initiation visits include activities such as verification that training was conducted and documented.

Site monitoring visits will be conducted by an authorized Medtronic representative to inspect study data, subjects' medical records, and CRFs in accordance with current ISO 14155 and ICH GCPs 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 Medtronic and/or designee(s) employed by Medtronic to review completed CRFs, EC/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 the Sponsor 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 maintain assurance that all study staff are trained on the CIP and use of the study devices. If the monitor discovers that an investigator is not complying with the signed Investigator Statement, the investigational plan, applicable laws, or any conditions of approval imposed by the reviewing EC/IRB or Regulatory Authority, the monitor will report to the Sponsor and take such steps necessary to promptly secure compliance. If compliance cannot be secured, the investigator's participation in the investigation may be terminated.

Because there are no required medications for this study or other subject-generated reporting requirements, monitoring of subject compliance is not applicable to this study.

A minimum of 80% source data verification is required, though a higher percentage of verification will be attempted. All ICFs and eligibility criteria are required to be 100% source-data verified.

Authorized Medtronic representatives will also conduct site close-out visits. Site close-out visits include activities such as ensuring site files are complete and accurate, essential documents are collected, and reminding the site of their study closure responsibilities.

15.2. Data Management

This study will utilize an electronic database and eCRF. All data requested on the eCRF are considered required. Data points not collected and/or recorded will be considered deviations unless otherwise specified. No data points will be collected directly on the eCRF.

In order to accurately collect all information, subject worksheets may also be provided for study specific data (e.g. specific nodule and procedure data points, etc.) not found in the medical records and will be considered the source document.

The Principal Investigator must ensure the accuracy and completeness of the recorded data and then provide his/her electronic signature on the appropriate CRFs. The Investigator's signature for specific CRFs 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 discrepancies will be created in the Oracle remote data capture (RDC) system and will be issued to the site for appropriate response. The site staff will be responsible for resolving all discrepancies in the database.

15.3. Direct Access to Source Data/Documents

The investigator(s)/institution(s) will permit inspection and study-related monitoring, audits, IRB/IEC review, and regulatory inspection(s), including direct access to source data/documents per applicable laws and regulations.

15.4. Confidentiality

All records identifying the subject will be kept confidential and, to the extent permitted by the applicable laws and/or regulations, will not be made publicly available.

Subject names will be kept confidential. Only the subject number will be recorded in the CRF, and if the subject name appears on any other document, it must be removed.

Study findings stored on a computer will be stored in accordance with local data protection laws. The subjects will be informed in writing that representatives of the sponsor, IRBs, or Regulatory Authorities may inspect their medical records to verify the information collected, and that all personal information

made available for inspection will be handled in strictest confidence and in accordance with local data protection laws.

Subjects will also be informed that information regarding the study that does not include subject identifiers will be posted on www.clinicaltrials.gov.

If the results of the trial are published, the subject's identity will remain confidential.

15.5. Liability

Medtronic maintains appropriate clinical study liability insurance coverage as required under applicable laws and regulations and will comply with applicable local law and custom concerning specific insurance coverage. If required, a clinical study insurance statement/certificate will be provided to the EC/IRB.

15.6. CIP Amendments

Should any amendment to the CIP be required, the CIP Author will collect and review all proposed updates. These will be incorporated as needed and approved per the CIP Approval Process, including EC/IRB approval and Regulatory Authority.

15.7. Record Retention

The investigator will maintain the records of the study including all pertinent correspondence, the CIP with any/all amendments, all correspondence with and approval from the EC/IRB, the clinical investigation agreement, the Investigator Agreement, individual subject records, and signed ICFs. Subject files and other source data must be maintained per required storage periods defined by the applicable laws.

Records may need to be maintained by the study investigator for a longer duration if agreed to in writing with Medtronic. All data and documents should be made available if requested by relevant authorities.

15.8. Publication and Use of Information

The Medtronic Publication and Authorship Policy is aligned with the International Committee of Medical Journal Editors (ICMJE) recommendations (www.icmje.org). The Sponsor will seek to publish, in appropriate peer-reviewed journals and scientific conferences, results of clinical studies where human subjects are involved, regardless of outcome. While study results are owned by the Sponsor, all data on which a publication is based will be made available to all authors as required for their participation in the publication process. Furthermore, data may be published or used by study investigators provided that such publication or use is in accordance with this protocol, the Medtronic Publication and Authorship Policy, and the Clinical Investigation Agreement. Investigators must submit a copy of all

manuscripts and/or abstracts to the Sponsor for review and comment at least 30 days prior to the planned submission. Medtronic acknowledges that its right to review and comment shall relate solely to the proprietary, licensing, and/or confidential rights Medtronic may have in such proposed publication, rather than whether such results and/or opinions are favorable to Medtronic.

The publication of substudies, post-hoc analyses, regional results, or single-center experiences based on multicenter clinical studies should not precede that of the primary multicenter publication, and should cite the primary publication whenever possible, as required by specific journal and scientific meeting guidelines.

Medtronic involvement in a publication (e.g., funding of the study; sponsor of the study; collection, analysis, and interpretation of data; professional writing assistance) must be disclosed according to journal-specific policies, submission requirements, and prevailing editorial standards, in addition to those specified by International Committee of Medical Journal Editors. Authors must ensure that an acknowledgement/disclosure statement is included in the body of the manuscript for Medtronic to review for accuracy. All authors must also disclose financial or personal affiliations that could be considered conflicts of interest as per journal/conference requirements.

To enable health care providers, payers, and patients access to the wealth of Medtronic's research, Medtronic will report its scientific data in accordance with the principles outlined in the Guidance Document on Registration and Reporting Results of Company-Sponsored Clinical Trials, Section 801 of the Food and Drug Administration Amendments Act (FDAAA 801) and the Final Rule for Clinical Trials Registration and Results Information Submission (42 CFR Part 11, January 18, 2017).

15.9. Suspension or Early Termination

At the time of a study close-out, the investigators will be notified by the sponsor. Appropriate notification and the final study report will be provided to EC/IRB and Regulatory Authority, if required per local laws and regulations.

Medtronic reserves the right to discontinue the study at any stage, with suitable written notice to the investigator, the reviewing EC/IRB, and applicable Regulatory Authority. Similarly, the investigator may withdraw from the study at any time, subject to providing written notification to Medtronic 30 days prior to the date they intend to withdraw. However, Medtronic and the investigator 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 shall be reported to Medtronic on the appropriate CRF.

15.10. Study Contact Information

Medtronic Clinical Research	Medtronic Medical Affairs
[redacted]	Jennifer Mattingley MD Medical Affairs Director MITG, Surgical Innovations, Lung Health 161 Cheshire Lane, Suite 100 Plymouth, MN 55441 [redacted]
Jennifer Wolvers Clinical Research Manager MITG, Surgical Innovations, Lung Health 161 Cheshire Lane; Suite 10 Plymouth, MN 55441 [redacted]	

15.11. Financial Information

Medtronic contracts with participating institutions/investigators through a Clinical Trial Agreement that defines the scope and responsibilities and associated compensation related to carrying out the obligations under a clinical study sponsored by Medtronic.

16. References

1. National Cancer Institute, Cancer Therapy Evaluation Program, United States Department of Health and Human Services, National Institutes of Health. Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0. Available at: https://ctep.cancer.gov/protocolDevelopment/electronic_applications/ctc.htm#ctc_50. Accessed January 23, 2018.
2. Ahmed M, Solbiati L, Brace CL, Breen DJ, Callstrom MR, Charboneau JW, et al. Image-guided tumor ablation: standardization of terminology and reporting criteria--a 10-year update. J Vasc Interv Radiol. 2014;25(11):1691-705 e4. doi: 10.1016/j.jvir.2014.08.027. PubMed PMID: 25442132.
3. National Comprehensive Cancer Network. Non–Small Cell Lung Cancer, Version 3.2018, NCCN Clinical Practice Guidelines in Oncology. National Comprehensive Cancer Network. 2018.
4. Hinshaw JL, Lubner MG, Ziemlewicz TJ, Lee FT, Jr., Brace CL. Percutaneous tumor ablation tools: microwave, radiofrequency, or cryoablation-what should you use and why? Radiographics. 2014;34(5):1344-62. doi: 10.1148/rg.345140054. PubMed PMID: 25208284.

5. Roberton BJ, Liu D, Power M, Wan JM, Stuart S, Klass D, et al. Pulmonary ablation: a primer. Can Assoc Radiol J. 2014;65(2):177-85. doi: 10.1016/j.carj.2013.01.003. PubMed PMID: 23942193.

6. Dupuy DE. Image-guided thermal ablation of lung malignancies. Radiology. 2011;260(3):633-55. doi: 10.1148/radiol.11091126. PubMed PMID: 21846760.

7. Dupuy DE, Zagoria RJ, Akerley W, Mayo-Smith WW, Kavanagh PV, Safran H. Percutaneous radiofrequency ablation of malignancies in the lung. AJR Am J Roentgenol. 2000;174(1):57-9. doi: 10.2214/ajr.174.1.1740057. PubMed PMID: 10628454.

8. Howington JA, Blum MG, Chang AC, Balekian AA, Murthy SC. Treatment of stage I and II non-small cell lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2013;143(5 Suppl):e278S-313S. doi: 10.1378/chest.12-2359. PubMed PMID: 23649443.

9. Lanuti M, Sharma A, Willers H, Digumarthy SR, Mathisen DJ, Shepard JA. Radiofrequency ablation for stage I non-small cell lung cancer: management of locoregional recurrence. Ann Thorac Surg. 2012;93(3):921-7; discussion 7-88. doi: 10.1016/j.athoracsur.2011.11.043. PubMed PMID: 22296982.

10. Casal RF, Tam AL, Eapen GA. Radiofrequency ablation of lung tumors. Clin Chest Med. 2010;31(1):151-63. doi: 10.1016/j.ccm.2009.08.021. PubMed PMID: 20172441.

11. de Baere T, Deschamps F. New tumor ablation techniques for cancer treatment (microwave, electroporation). Diagnostic and interventional imaging. 2014;95(7-8):677-82. doi: 10.1016/j.diii.2014.04.001. PubMed PMID: 24818966.

12. Howk K, Ladtkow C, Peterson D, Cafaro A. Consistent and Predictable Spherical Ablation Shape in Both Liver and Lung: Performance of the Emprint Ablation System with Thermosphere Technology in an In Vivo Porcine Model [Poster 129]. J Vasc Interv Radiol. 2015;26(5):e89-e90.

13. Howk K, Ladtkow C, Peterson D, Cafaro A. Performance of the Emprint™ Ablation System in an In Vivo Porcine Lung Model: Correlation between CT and Gross Measurements [Poster 131]. J Vasc Interv Radiol. 2015;26(5):e91.

14. Alonzo M, Bos A, Bennett S, Ferral H. The Emprint Ablation System with Thermosphere Technology: One of the Newer Next-Generation Microwave Ablation Technologies. Semin Intervent Radiol. 2015;32(4):335-8. doi: 10.1055/s-0035-1564811. PubMed PMID: 26622094; PubMed Central PMCID: PMC4640908.

15. Ierardi AM, Coppola A, Lucchina N, Carrafiello G. Treatment of lung tumours with high-energy microwave ablation: a single-centre experience. Medical oncology. 2017;34(1):5. doi: 10.1007/s12032-016-0861-6. PubMed PMID: 27900591.

16. Gex G, Pralong JA, Combescure C, Seijo L, Rochat T, Soccal PM. Diagnostic yield and safety of electromagnetic navigation bronchoscopy for lung nodules: a systematic review and meta-analysis. Respiration. 2014;87(2):165-76. doi: 10.1159/000355710. PubMed PMID: 24401166.

17. Heerink WJ, de Bock GH, de Jonge GJ, Groen HJ, Vliegenthart R, Oudkerk M. Complication rates of CT-guided transthoracic lung biopsy: meta-analysis. Eur Radiol. 2017;27(1):138-48. doi: 10.1007/s00330-016-4357-8. PubMed PMID: 27108299; PubMed Central PMCID: PMC5127875.

18. Berber E. The first clinical application of planning software for laparoscopic microwave thermosphere ablation of malignant liver tumours. HPB (Oxford). 2015;17(7):632-6. doi: 10.1111/hpb.12423. PubMed PMID: 25980481; PubMed Central PMCID: PMC4474511.

19. Ierardi AM, Mangano A, Floridi C, Dionigi G, Biondi A, Duka E, et al. A new system of microwave ablation at 2450 MHz: preliminary experience. Updates in surgery. 2015;67(1):39-45. Epub March 17. doi: 10.1007/s13304-015-0288-1. PubMed PMID: 25776064.

20. De Cobelli F, Marra P, Ratti F, Ambrosi A, Colombo M, Damascelli A, et al. Microwave ablation of liver malignancies: comparison of effects and early outcomes of percutaneous and intraoperative approaches with different liver conditions: New advances in interventional oncology: state of the art. Medical oncology. 2017;34 (4) (no pagination)(49). doi: 10.1007/s12032-017-0903-8.

21. Floridi C, Radaelli A, Pesapane F, Fumarola EM, Lecchi M, Agostini A, et al. Clinical impact of cone beam computed tomography on iterative treatment planning during ultrasound-guided percutaneous ablation of liver malignancies. Medical oncology. 2017;34 (6) (no pagination)(113). doi: 10.1007/s12032-017-0954-x.

22. Takahashi H, Kahramangil B, Berber E. Local recurrence after microwave thermosphere ablation of malignant liver tumors: Results of a surgical series. Surgery. 2017. doi: 10.1016/j.surg.2017.10.026.

23. Vogl TJ, Basten LM, Nour-Eldin NA, Kaltenbach B, Bodelle B, Wichmann JL, et al. Evaluation of microwave ablation of liver malignancy with enabled constant spatial energy control to achieve a predictable spherical ablation zone. International journal of hyperthermia : the official journal of European Society for Hyperthermic Oncology, North American Hyperthermia Group. 2017:1-9. doi: 10.1080/02656736.2017.1358408. PubMed PMID: 28774210.

24. Vogl TJ, Panahi B, Albrecht MH, Naguib NNN, Nour-Eldin NA, Gruber-Rouh T, et al. Microwave ablation of pancreatic tumors. Minim Invasive Ther Allied Technol. 2018;27(1):33-40. doi: 10.1080/13645706.2017.1420664. PubMed PMID: 29278340.

25. Steinfort DP, Einsiedel P, Irving LB. Radiation dose to patients and clinicians during fluoroscopically-guided biopsy of peripheral pulmonary lesions. Respir Care. 2010;55(11):1469-74. Epub 2010/10/29. PubMed PMID: 20979674.

26. Hohenforst-Schmidt W, Banckwitz R, Zarogoulidis P, Vogl T, Darwiche K, Goldberg E, et al. Radiation exposure of patients by cone beam CT during endobronchial navigation-a phantom study. J Cancer. 2014;5(3):192.

17. Appendices

17.1. User Manual

See attached document, “Appendix 17.1_User Manual” for the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology Bronchoscopic Ablation Instructions for Use (CA108L1).

17.2. Product Label

See attached document, “Appendix 17.2_Product Label” for the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology Bronchoscopic Ablation Shipping Label (CA108L1).

17.3. Bronchoscopic Ablation Patient Satisfaction and Pain Survey

See attached document, “Appendix 17.3_Patient Satisfaction and Pain”

17.4. Quality of Life Questionnaire

See attached document, “Appendix 17.4_Quality of Life (EQ-5D)”

17.5. NAVABLATE Adverse Event Reference List

See attached document, “Appendix 17.5_NAVABLATE Adverse Event Reference List”

17.6. Sample Informed Consent Form

See attached document, “Appendix 17.6_NAVABLATE Sample ICF”

18. Version History

Version History	Summary of Changes	Author(s)/Title
1.0	• Not applicable (new document)	Jennifer Wolvers, Principal Clinical Research Specialist Kristin Hood, Senior Principal Medical Writer
2.0	• To Appendix 17.3, added MRC Breathlessness Scale	Jennifer Wolvers, Principal Clinical

		Research Specialist Kristin Hood, Senior Principal Medical Writer
3.0	Requested updates per radiation expert. • To Table 1: Added standard of care CT scan at baseline, noting this is already done prior to consent. • Modified section 10.1.3 “Radiation Exposure” to be more generalizable.	Jennifer Wolvers, Principal Clinical Research Specialist Kristin Hood, Senior Principal Medical Writer
4.0	• Updated to most current version of 056-F275, version A, Clinical Investigation Plan Template (no required changes other than updating footnote). • Updated names, addresses, and titles of sponsor and study contacts on Title page, and in Section 3 and 15.10 • Added name and address of co-lead principal investigator (Dr. Calvin Ng) to the title page • Added most current IFU to Appendix 17.1 • Corrected typo in Appendix 17.5, NAVABLATE Adverse Event Reference List • Added Section 17.6, Sample Informed Consent Form The following updates were made for compliance to the European Union Medical Device Regulation (EU MDR): • Added name and address of Europe Authorized Representative to the title page, Section 1, and Section 3. • Added statement of compliance to the EU MDR to Section 1 and Section 14.1 • Added EU MDR, IFU, and PMV to Section 2.1 • Added statement to Section 3	Jennifer Wolvers, Clinical Research Manager Kristin Hood, Senior Principal Medical Writer

	regarding device use per the IFU • Added statement to Section 3 that there is no required number of subjects and 20 is the approximated minimum • Added statement to Section 7.1 indicating that the device is used for the ablation of lung tissue • Added statement to Section 7.1 regarding anticipated product changes • Added statement to Section 7.4 that products are packaged and labeled accordingly • Added statement to Section 7.5 regarding the population of patients being evaluated • Statement added to Section 7.6 allowing use of the CrossCountry™ Transbronchial Access Tool to obtain access • Added statement that no CIP waivers will be granted to Section 9.10 • Added statement to Section 9.10 to address how study deviations will be reported to the Regulatory Authority • Added statement to Section 9.11 indicating that standard of care will be followed for all subjects after withdrawal, discontinuation, or completion of the study follow-ups • Added statement to Section 10.1 that the study has been designed to have as little foreseeable risk as possible for patients • Added foetal events Serious Adverse Event definition in Section 11.1.2 • Added definition of an anticipated serious adverse device effect to Section 11.1.5 • Added statement to Section 11.2.1	

	that applicable events will be reported to PMV, who will report necessary events to Regulatory Authorities • Updated record retention period to be per applicable laws rather than defined timeframe in Section 15.7 • Statement added to Section 15.9 regarding the notification of the final study report • Added Section 15.11 regarding financial information	

COVIDIEN™

REF CA108L1

Emprint™

Ablation Catheter Kit with Thermosphere™ Technology

Bronchoscopic Ablation

en **Instructions for Use**

fr **Instructions d'utilisation**

de **Gebrauchsanleitung**

es **Instrucciones de uso**

it **Istruzioni per l'uso**

nl **Gebruiksaanwijzing**

sv **Bruksanvisning**

da **Brugsanvisning**

no **Bruksanvisning**

Symbols on Product and Packaging

The following symbols may appear on product or packaging:

Sterile using ethylene oxide

Not made with natural rubber latex


Single use

Federal law (USA) restricts this device to sale by or on the order of a physician

Do not resterilize


Do not use if package is opened or damaged


Type BF applied part


Consult instructions for use


Keep dry

Catalog number


Manufacturer


Use by

Batch code


Date of manufacture


China RoHS (reduction of hazardous substances)

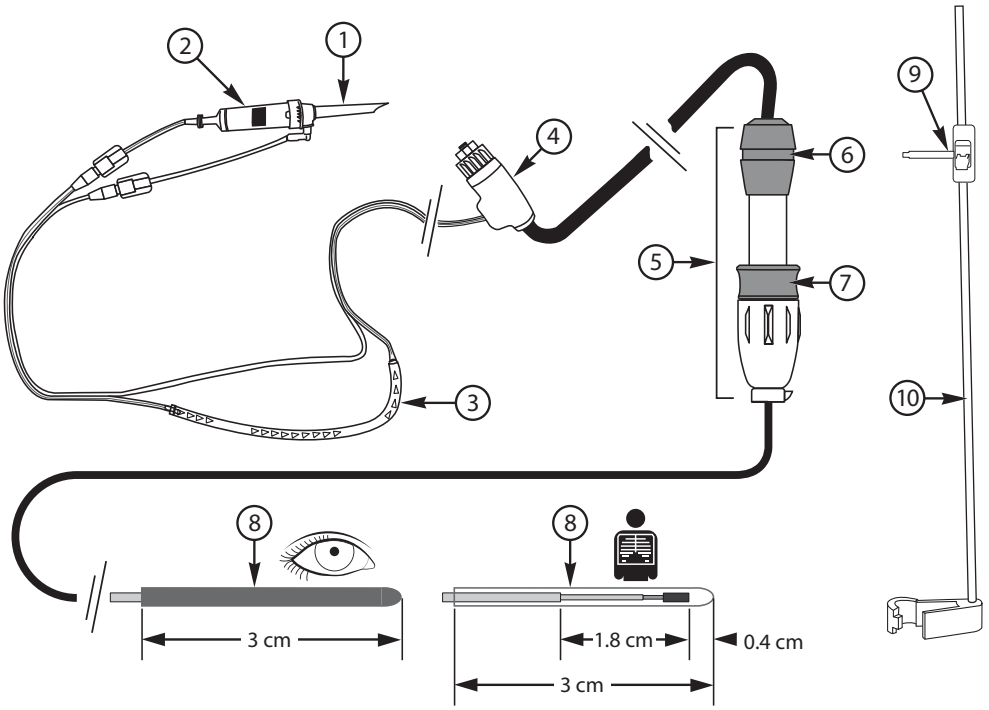
Authorized representative in the European Community


CE mark. Designates that the product is authorized for sale in European countries

en

REF CA108L1 Emprint™ Ablation Catheter Kit with Thermosphere™ Technology

Bronchoscopic Ablation



Device Description

Emprint™ Ablation Catheter Kit with Thermosphere™ Technology is for use with the Emprint™ Ablation System with Thermosphere™ Technology for the ablation of lung tissue.

1. Intravenous (IV) bag spike
2. Drip chamber
3. Pump tubing (orange)
4. Generator connector
5. Ablation catheter handle
6. Top groove
7. Control ring
8. Radiating section
9. Clip
10. Rail

The Emprint ablation catheter kit is designed for use with:

- Emprint Ablation Generator (required)
- Emprint Ablation Pump (required)
- Emprint Ablation Cart (required)
- Edge™ or Edge™ Firm Tip Extended Working Channel (required)
- Edge Bronchoscope Adapter (required)
- Ablation Footswitch (optional)
- 1 liter saline (required)

Indication for Use

The Emprint™ Ablation System with Thermosphere™ Technology is intended for use in percutaneous, laparoscopic, endoscopic, and intraoperative coagulation (ablation) of soft tissue, including partial or complete ablation of non-resectable liver tumors.

The Emprint™ Ablation System with Thermosphere™ Technology is not intended for use in cardiac procedures.

Contraindications

Do not defibrillate a patient with an ablation catheter inserted. Completely remove the catheter from the patient prior to defibrillation.

Microwave ablation procedures are not recommended for pregnant patients or patients with cardiac pacemakers or implanted electronic devices. Potential risks to the patient or fetus have not been evaluated.

Parts of the body of the patient containing metallic implants should not be treated unless specialized medical advice is obtained.

Warning

The ablation catheter kit is supplied sterile. Do not resterilize.

Do not use this device if it appears to be damaged.

Warning

This device has been validated and warranted for single-use only. Any re-use, reprocessing, or re-sterilization could result in device failure causing patient or user injury, illness, or death. Re-use, reprocessing, or re-sterilization could cause contamination of the device, which could result in patient infection.

Be careful when creating ablation zones near critical structures including but not limited to large vasculature, heart, pleural boundary, esophagus, ductal structures, and the diaphragm.

Do not touch the catheter radiating section at any time during the application of energy.

During energy delivery, ensure that the ablation catheter radiating section does not come in contact with tissue other than the intended target, as inadvertent thermal injury may occur.

Do not activate the ablation catheter while the radiating section is in contact with metal objects or instruments, as inadvertent thermal injury may occur.

Fire/Explosion Hazard: Do not use the Emprint ablation system in potentially flammable or explosive room environments.

The following substances will contribute to increased fire and explosion hazards in the operating room:

- Flammable substances such as flammable anesthetics or alcohol-based skin prepping agents and tinctures
- Oxygen enriched atmospheres
- Oxidizing agents such as nitrous oxide (N_2O) atmospheres

Heating associated with microwave energy can provide an ignition source. Observe fire precautions at all times. When using microwave energy in the same room with any of these substances or gases, prevent their accumulation or pooling under surgical drapes, or within the area where microwave procedures are performed.

Do not look into or place the ablation catheter radiating section near eyes or testes when energized, as this may result in burns or other injuries to the patient or user.

Before use with a bronchoscope, verify compatibility and any criteria for safe use defined in the bronchoscope's instructions for use.

Ensure that the bronchoscope is either a Type BF or Type CF applied part.

When energized bronchoscopes are used with energized endotherapy devices, patient leakage currents may be additive.

Precaution

The Emprint ablation catheter kit should only be used by clinicians and staff properly trained in the use of this technology and its associated warnings and cautions. Clinicians should also be trained in the use of image guidance technology such as computed tomography (CT) or cone beam CT for the placement of ablation devices.

Storage

- Store ablation catheters away from moisture and direct heat.
- Discard products that have passed the use by date displayed on product packaging.

Inspection of Package Contents

Examine the package carefully before opening to confirm its integrity and that the use by date has not passed. Do not use the device if the package is damaged or opened or if the use by date has passed.

Instructions for Use

Procedure Setup

Precaution

The Emprint ablation generator, Emprint ablation pump, Emprint ablation catheter kit, and Emprint ablation cart are designed for use as a single system.

Failure to understand and follow provided instructions may result in improper functioning of the system and cause injury to the patient or user.

The Emprint ablation cart, including the isolation transformer, must be included in the system setup with the Emprint ablation catheter kit.

Important

Refer to the *Emprint™ Ablation System with Thermosphere™ Technology User's Guide* for detailed instructions regarding proper setup and activation of the Emprint generator and pump.

For ease of use, only remove portions of the device from the packaging tray as instructed below. The ablation catheter packaging is designed so that the catheter components can remain in the packaging until each is needed.

1. Confirm that the Emprint generator and Emprint pump are set up according to the *Emprint™ Ablation System with Thermosphere™ Technology User's Guide*.
2. Plug in the Emprint system.
3. Remove the rail from the packaging tray and then disconnect the tray lid.

4. Place the ablation catheter packaging on top of the Emprint cart as shown in *Figure 1*.

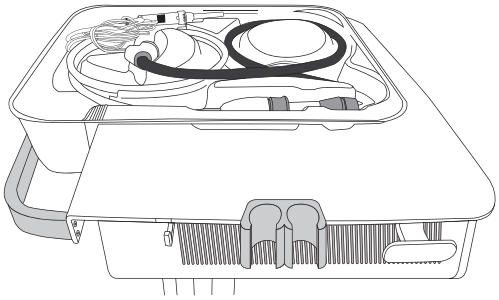


Figure 1

5. Hang a 1L or larger, room temperature sterile saline bag on the Emprint cart. A hook is provided on the left side of the cart.
6. Remove the white cap from the IV bag spike on the device tubing.
7. Fully insert the IV bag spike into the port on the saline bag. Confirm the IV bag spike extends well into the main reservoir of the IV bag as shown in *Figure 2*.

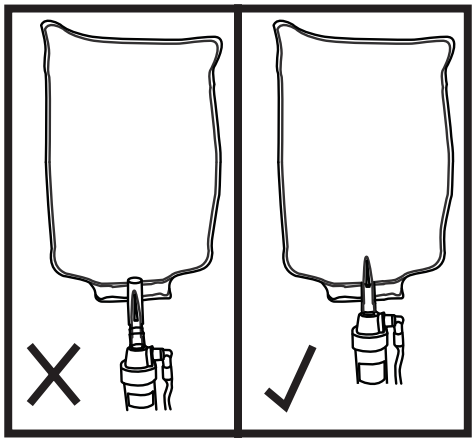


Figure 2

8. Prime the drip chamber by gently squeezing its sides until it is approximately half full of saline. The blue indicator should be floating near the surface of the saline.
9. Open the clear pump-head door and insert the orange pump tubing under the pump roller and into the pump roller clamps. Match the arrows on the pump tubing with the arrows on the pump head.
10. Close the pump-head cover completely. If the cover is not completely closed, the pump will not operate.
11. Grasp and push the generator connector to attach it to the front panel of the Emprint generator.
12. Activate the pump by pressing the activation switch on the pump's front panel.
13. Allow the pump to fully prime the ablation catheter with saline before continuing with the procedure. The catheter is fully primed when there are no air bubbles observed entering the IV bag.

Precaution

When the pump is activated, ensure that saline flowing to the catheter is constantly dripping into the drip chamber. The pump circulates saline through the ablation catheter and back into the IV bag. Failure to circulate saline may result in heating of the ablation catheter that could prevent the system from operating properly.

Precaution

If the pump is active and the saline is not flowing, the tubing may be damaged or blocked.

Stop the pump and perform the following troubleshooting steps:

- Confirm that the direction of the orange tubing arrows align with the pump head arrows.
- Confirm that the IV bag spike is inserted well into the main reservoir of the IV bag (*Figure 2*).
- Remove and reinsert the orange pump tubing to ensure proper seating of the pump tubing in the pump roller clamps.

Restart the pump. If saline is still not flowing, replace the ablation catheter.

If any portion of the setup is leaking after troubleshooting, replace the ablation catheter.

14. On the Emprint generator panel, press the power switch to turn on the generator.

Warning

Do not activate microwave energy until setup is complete and the ablation catheter radiating section is fully inserted into tissue.

Important

If the Emprint generator displays an error during startup, confirm that the ablation catheter generator connector is properly mated to the generator front panel. Refer to the troubleshooting information in the *Emprint™ Ablation System with Thermosphere™ Technology User's Guide* for additional information.

Placing the Ablation Catheter

1. Place the Edge extended working channel in the desired location and confirm with imaging.
2. Tighten the Edge bronchoscope adapter prior to inserting the ablation catheter.
3. Attach the rail to the bronchoscope adapter as shown in *Figure 3*. Align the ridge on the bronchoscope adapter with the indent on the rail and snap into place.

Precaution

Do not attempt to manually bend or reshape the ablation catheter. Be careful not to kink the device as product damage or malfunction may result.

4. Depress the latch on the ablation catheter handle and remove the protective tube. Check the ablation catheter radiating section and ensure that there are no rough surfaces, sharp edges, or protrusions.
5. Using short, 2 cm strokes, insert the ablation catheter into the extended working channel. Observe the last 3 cm of the ablation catheter insertion using image guidance to ensure that the ablation catheter:
   - remains sheathed in the extended working channel.
   - is not severely bent or broken during insertion.
6. Insert the ablation catheter into the extended working channel until the ablation catheter handle latch locks with the extended working channel handle. When fully inserted, the ablation catheter tip may protrude slightly from the distal end of the extended working channel.
7. Slide the ablation catheter clip onto the rail.
8. Attach the ablation catheter clip to the top groove on the ablation catheter handle. *Refer to Figure 3*.
9. Verify that a portion of the rail is extending above the top of the clip. This will ensure that the extended working channel is adequately extended outside of the bronchoscope after unsheathing.
10. Lock the ablation catheter clip to fix the ablation catheter to the bronchoscope. The device setup should now look like the setup shown in *Figure 3, A* (control ring down and lock symbols visible).
11. Open the bronchoscope adapter to allow movement of the extended working channel in order to unsheathe the ablation catheter.
12. While using image guidance to monitor the ablation catheter's position, grasp and slide the ablation catheter control ring upward to retract the extended working channel and unsheathe the ablation catheter radiating section. Slide the control ring up until it clicks into place. *Refer to Figure 3, B and B1*.
13. Use image guidance to confirm that:
    - the distal end of the extended working channel is extended beyond the bronchoscope (the dark blue portion of the extended working channel should be visible on the bronchoscope view).
    - the ablation catheter radiating section is outside of the extended working channel.
    - the ablation catheter radiating section is fully inserted into the target tissue.

Precaution

Failure to ensure that the extended working channel and ablation catheter radiating section is adequately extended beyond the bronchoscope may damage the bronchoscope.

14. If any ablation catheter forward adjustment is required, pull the control ring down to sheathe the ablation catheter before attempting to adjust the location. *Refer to Figure 3, A1*.
15. Tighten the bronchoscope adapter.

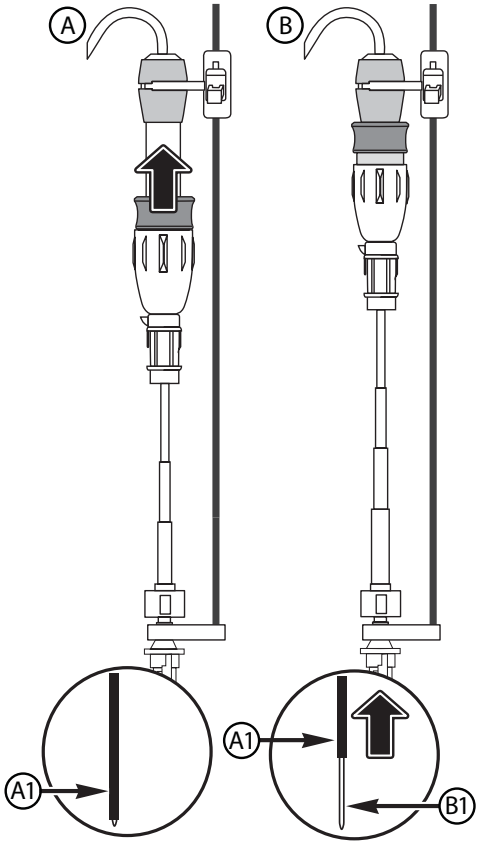


Figure 3

Precaution

Full retraction of the extended working channel is necessary to expose the entire ablation catheter radiating section to the tissue. Ensure that the ablation catheter handle locks into the unsheathed position prior to activation as shown in *Figure 3*, B.

The ablation catheter is not designed to penetrate tissue beyond the Edge extended working channel. Proper use requires retraction of the extended working channel to unsheathe the ablation catheter radiating section.

Activating the Ablation Catheter

Warning

Confirm that the ablation catheter radiating section is in direct contact with target tissue or tightly wedged into a peripheral airway (no air around the radiating section). Failure to do so may result in unintended thermal injury or alter the ablation zone.

1. Set the Emprint generator's power setting and activation time. Refer to the *Ablation Zone Examples* section for guidance on power and time settings.

Important

If the power and time displays do not adjust, confirm proper connection between the ablation catheter generator connector and the Emprint generator front panel. Note that the Emprint ablation catheter limits the Emprint generator to a maximum of 100 watts and 10 minutes.

If the Emprint generator displays a symbol, refer to the *Emprint™ Ablation System with Thermosphere™ Technology User's Guide* for symbol descriptions and instructions.

2. Press the Emprint generator START/STOP button or press the footswitch to activate microwave energy to the ablation catheter.

Important

Pressing the START/STOP button immediately stops energy delivery in an emergency.

3. Use image guidance to:
   - confirm that the ablation catheter radiating section is not displaced during activation.
   - monitor ablation zone formation.

Removing the Ablation Catheter

1. When ablation catheter energy delivery is complete, open the bronchoscope adapter to allow movement of the extended working channel.
2. Grasp and pull down the control ring until it clicks into place to sheathe the radiating section.
3. Tighten the bronchoscope adapter.
4. Unlock the ablation catheter clip, disconnect the clip from the top groove, and remove it from the rail.
5. Depress the latch on the ablation catheter and remove the ablation catheter from the extended working channel.

Warning

Do not clean the ablation catheter with any sharp or abrasive objects as damage to the catheter may occur, potentially resulting in saline leakage and possible patient injury.

6. If ablating another target area, ensure that no rough surfaces are present on the ablation catheter prior to re-insertion.
7. To avoid an Emprint generator temperature shutoff error, connect a new, room temperature 1L or larger sterile saline bag to the system prior to every ablation.

After a Procedure

1. Verify that the Emprint generator is not delivering microwave energy to the ablation catheter.
2. Press the pump activation switch to turn off the pump operation.
3. Press the Emprint generator power switch to turn it off.
4. Open the pump head and remove the pump tubing.
5. Disconnect the used ablation catheter from the Emprint generator. Twist and pull the generator connector to remove it from the front panel.
6. Dispose of the ablation catheter and saline IV bag in accordance with hospital or clinic protocol.

Further Information

The *Emprint™ Ablation System with Thermosphere™ Technology User's Guide* provides additional information about the Emprint ablation system components. Refer to the user's guide for information regarding:

- Using the system
- Other component functions
- Disposal
- Troubleshooting
- Technical specifications
- Technical support

Ablation Zone Examples

The ablation zone results examples contained in *Table 1* were developed using the ablation catheter kit in an in vivo porcine lung. The table includes the ablation diameter (A), height (B), and distance from the tip (C) versus time (MM:SS) for three power levels (45 watts, 75 watts, and 100 watts).

The circular areas in *Figure 4* represent the zone of tissue coagulation created around the ablation catheter radiating section. The shape and size of ablation zones may vary in clinical settings.

	45 W			75 W			100 W		
A	MM:SS	B	C	MM:SS	B	C	MM:SS	B	C
1.6 cm	2:00	2.8 cm	0.6 cm						
1.9 cm	3:00	3.0 cm	0.7 cm	2:00	3.1 cm	0.8 cm			
2.2 cm	4:30	3.3 cm	0.8 cm	2:30	3.3 cm	0.9 cm			
2.5 cm	7:30	3.5 cm	0.9 cm	3:30	3.6 cm	0.9 cm	2:30	3.3 cm	0.7 cm
2.7 cm	10:00	3.6 cm	1.0 cm	4:30	3.8 cm	1.0 cm	3:00	3.5 cm	0.8 cm
2.9 cm				5:30	3.9 cm	1.1 cm	4:00	3.7 cm	0.8 cm
3.1 cm				7:00	4.0 cm	1.1 cm	5:00	3.9 cm	0.9 cm
3.3 cm				9:00	4.1 cm	1.1 cm	7:00	4.0 cm	1.0 cm
3.4 cm				10:00	4.2 cm	1.1 cm	8:30	4.1 cm	1.0 cm
3.5 cm							10:00	4.2 cm	1.0 cm

Table 1

In Vivo Porcine Lung

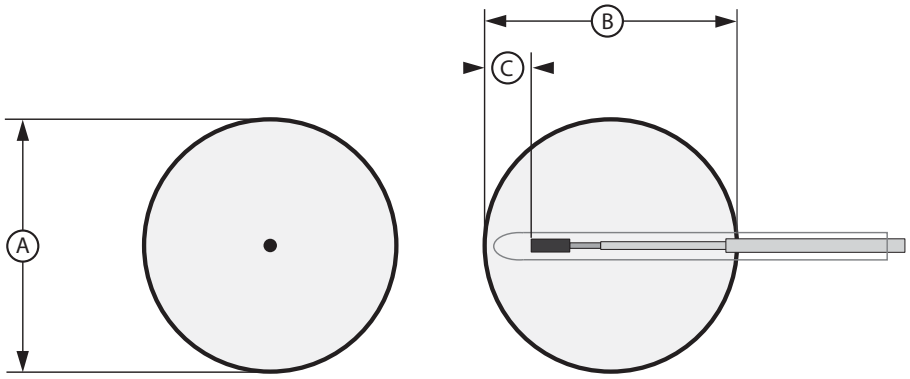


Figure 4

Do not resterilize

Not made with natural rubber latex

Single use

Rx ONLY

Consult instructions for use

Keep dry

CE
0086

Document No. DLB00794-01 Rev. A
Part No. PLB00555-01 Rev. A

Covidien llc,
15 Hampshire Street
Mansfield, MA 02048 USA.

EC REP Covidien Ireland Limited
IDA Business and Technology Park, Tullamore.

Made in USA. Printed in USA.

www.covidien.com

REV 2016-06

PRODUCT INFORMATION	
Product Brand	Emprint™
Product Descriptor 1	Ablation Catheter Kit with Thermosphere™ Technology
Product Descriptor 2	Bronchoscopic Ablation
Catalog Number	CA108L1
Size	n/a

LABEL INFORMATION	
Art Specification	DLB00943-01 Rev. A
Part Number	PLB00678-01 Rev. A
GTIN	10884521543461
Product Quantity	n/a
Label Applied to	Outer Shipping Box
Artwork Key	↔ Measurement Die
Print Process	On-Demand
Corner Radius	n/a
Label Size	4″ width x 6″ height

INCLUDED LANGUAGES	
EN	ENGLISH
FR	FRENCH-EU
PT	PORTUGUESE-BRAZIL
DE	GERMAN
ES	SPANISH-EU
IT	ITALIAN
NL	DUTCH
SV	SWEDISH
RU	RUSSIAN
ZH	CHINESE-SIMPLIFIED
CS	CZECH
DA	DANISH
KO	KOREAN
NO	NORWEGIAN
PL	POLISH
TR	TURKISH
ZH-T	CHINESE-TRADITIONAL

LABEL CALLOUTS	
①	Catalog number
②	Batch code*
③	Use by YYYY-MM-DD*
④	Date of manufacture YYYY-MM-DD*
⑤	GS1-128 Barcode* (01) GTIN* (17) Use by YYMMDD* (10) Batch code*
⑥	• Label part number • Date of revision

*Not included in the png file – added during on-demand label printing.

COVIDIEN 15 Hampshire Street, Mansfield, MA 02048

GBU-SPECIFIC INFORMATION	
Graphic Designer	David Klein

TECHNICAL INFORMATION	
Application/ Version	InDesign/CC
Placed Images	Embedded
Fonts Used	Myriad Pro
File Exported for Printing	PNG • Grayscale • 300 dpi • No transparency

COMMENTS
Please review the accompanying PNG file that is used to print the label.

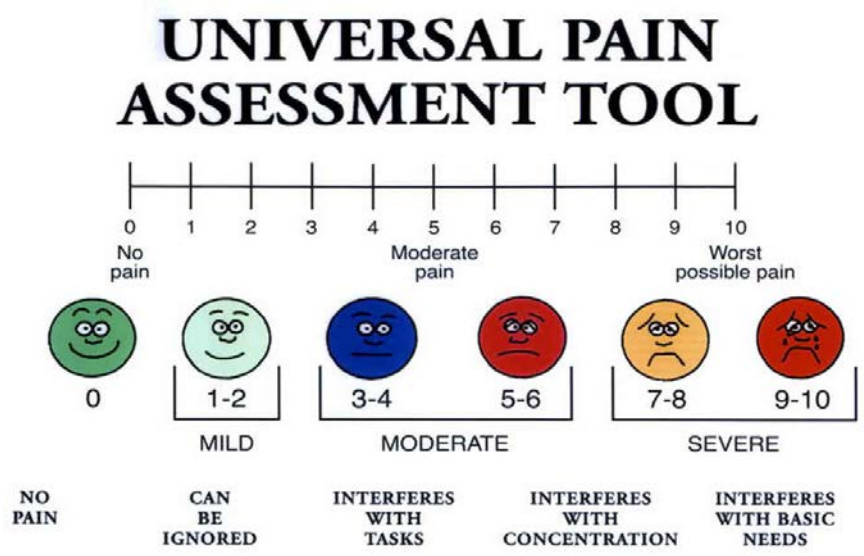
PRINTER NOTES

Subject # _____

Bronchoscopic Ablation Patient Pain and Satisfaction Survey

As a participant in the NAVABLATE study, you are being asked to complete this survey. Please take a few minutes to complete the form. The information you provide will be used to evaluate patients' satisfaction with the Bronchoscopic Ablation procedure.

Date Survey Completed: _____



What level of <u>pain or discomfort</u> did you experience because of the Bronchoscopic Ablation procedure:	***Using the scale above as a guide, please circle the number that best fits your answer:***										
Immediately after the Bronchoscopic Ablation procedure?	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
One week after the Bronchoscopic Ablation procedure?	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
One month after the Bronchoscopic Ablation procedure?	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**

Grade	**Degree of breathlessness related to activities (MRC Breathlessness Scale)***
1	Not troubled by breathlessness except on strenuous exercise
2	Short of breath when hurrying on the level or walking up a slight hill
3	Walks slower than most people on the level, stops after 1.5 kilometers or so, or stops after 15 minutes walking at own pace
4	Stops for breath after walking about 100 meters or after a few minutes on level ground
5	Too breathless to leave the house, or breathless when undressing

What level of <u>breathlessness</u> did you experience because of the Bronchoscopic Ablation procedure:	***Using the scale above as a guide, please circle the number that best fits your answer:***				
Immediately after the Bronchoscopic Ablation procedure?	**1**	**2**	**3**	**4**	**5**
One week after the Bronchoscopic Ablation procedure?	**1**	**2**	**3**	**4**	**5**
One month after the Bronchoscopic Ablation procedure?	**1**	**2**	**3**	**4**	**5**

Subject # _____

	Please circle the number that best fits your answer				
	Extremely Unlikely	Unlikely	Neutral	Likely	Extremely Likely
How likely would you be <u>willing to have</u> an Bronchoscopic Ablation procedure performed again if necessary?	**1**	**2**	**3**	**4**	**5**
How likely would you <u>recommend</u> the Bronchoscopic Ablation procedure to family and friends if necessary?	**1**	**2**	**3**	**4**	**5**

	Please circle the number that best fits your answer				
	Totally Dissatisfied	Dissatisfied	Neutral	Satisfied	Extremely Satisfied
Overall, how <u>satisfied</u> were you with the Bronchoscopic Ablation procedure?	**1**	**2**	**3**	**4**	**5**

Printed name of person completing this worksheet: _____

Signature: _____ **Date**: _____

* Used with the permission of the Medical Research Council and adapted to include metric distance units.
References: 1959 MRC Dyspnoea scale / MRC Breathlessness scale London, UK: Medical Research Council, Accessed: June 1, 2018. Available at: https://mrc.ukri.org/research/facilities-and-resources-for-researchers/mrc-scales/mrc-dyspnoea-scale-mrc-breathlessness-scale/, and
Stenton C. The MRC breathlessness scale. Occupational medicine (Oxford, England). 2008; 58(3):226-227.

Health Questionnaire

English version for the UK

(Validated for Ireland)

By placing a tick in one box in each group below, please indicate which statements best describe your own health state today.

Mobility

I have no problems in walking about ❑

I have some problems in walking about ❑

I am confined to bed ❑

Self-Care

I have no problems with self-care ❑

I have some problems washing or dressing myself ❑

I am unable to wash or dress myself ❑

Usual Activities *(e.g. work, study, housework, family or leisure activities)*

I have no problems with performing my usual activities ❑

I have some problems with performing my usual activities ❑

I am unable to perform my usual activities ❑

Pain / Discomfort

I have no pain or discomfort ❑

I have moderate pain or discomfort ❑

I have extreme pain or discomfort ❑

Anxiety / Depression

I am not anxious or depressed ❑

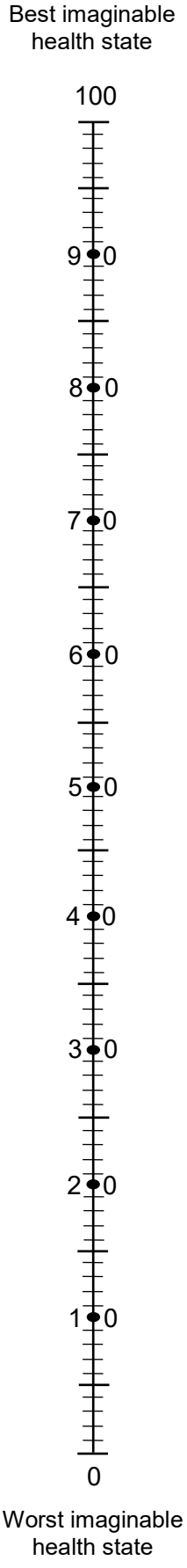
I am moderately anxious or depressed ❑

I am extremely anxious or depressed ❑

To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.

We would like you to indicate on this scale how good or bad your own health is today, in your opinion. Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad your health state is today.

Your own health state today



NAVABLATE Adverse Event Reference List

Table of Contents

Common Terminology Criteria for Adverse Events (CTCAE)

A set of criteria for the standardized classification of adverse effects of drugs used in cancer therapy. The CTCAE system is a product of the US National Cancer Institute Cancer Therapy Evaluation Program. This protocol will use Version 5.0 (published 27-NOV-2017), available at https://ctep.cancer.gov/protocolDevelopment/electronic_applications/ctc.htm#ctc_50https://ctep.cancer.gov/protocolDevelopment/electronic_applications/ctc.htm#ctc_50

Instrumental Activities of Daily Living

For the purpose of defining CTCAE grade, instrumental activities of daily living (ADL) refers to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.

Self-Care Activities of Daily Living

For the purpose of defining CTCAE grade, self-care activities of daily living (ADL) refer to bathing, dressing and undressing, feeding self, using the toilet, taking medications, and not bedridden.

Adverse Event and Device Deficiency Definitions

Adverse Event (AE)

An Adverse Event (AE) 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 investigational medical device.*

*For the purposes of this clinical study, AE definitions will be ISO 14155:2011 compliant with the following exception: only those adverse events that are related to the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology, accessory devices, or study procedures will be captured and reported.

NOTE 1: This definition includes events related to the investigational medical device or the comparator.

NOTE 2: This definition includes events related to the procedures involved.

NOTE 3: For users or other persons, this definition is restricted to events related to investigational medical devices.

Serious Adverse Event (SAE)

For the purposes of this study, a Serious Adverse Event* is an adverse event that has

1. Led to death,

2. Led to serious deterioration in the health of the subject, that either resulted in
    a. A life-threatening illness or injury, or
    b. A permanent impairment of a body structure or a body function, or
    c. In-patient or prolonged hospitalization, or
    d. Medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function.
3. led to fetal distress, fetal death or a congenital abnormality or birth defect

NOTE 1: This includes device deficiencies that might have led to a serious adverse event if a) suitable action had not been taken or b) intervention had not been made or c) if circumstances had been less fortunate. These are handled under the SAE reporting system.

NOTE 2: 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.

*For the purposes of this clinical study, SAE definitions will be ISO 14155:2011 compliant with the following exception: only those SAEs that are related to the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology, accessory devices, or study procedures will be captured and reported.

Adverse Device Effect (ADE)

An Adverse Device Effect (ADE) is an adverse event related to the use of the investigational medical device (the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology).

NOTE 1: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device.

NOTE 2: This definition includes any event resulting from use error or from intentional misuse of the investigational medical device.

Serious Adverse Device Effect (SADE)

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

Unanticipated Serious Adverse Device Effect (USADE)

An Unanticipated Serious Adverse Device Effect (USADE) is defined as serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current version of the Risk Management Report.

Device Deficiency

Inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance.

Note: Device deficiencies include malfunctions, use errors, and inadequate labelling.

Adverse Event Relationship and Outcome Classifications

Adverse Event Relationship Classification

Causality assessments define the relationship between the use of the medical device (including the procedure) and the occurrence of each adverse event. During causality assessment activity, clinical judgment shall be used and the relevant documents, such as the MDR Reportable Event Trend & Risk Analysis Report shall be consulted, as all the foreseeable serious adverse events and the potential risks are listed and assessed there. The presence of confounding factors, such as concomitant medication/treatment, the natural history of the underlying disease, other concurrent illness or risk factors shall also be considered.

Each AE and SAE will be classified according to five different levels of causality. The following definitions will be used to assess the relationship of the adverse event to the investigational medical device (the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology), accessory devices, or procedures:

- *Not related*: Relationship to the device or procedures can be excluded when:
  - the event is not a known side effect of the product category the device belongs to or of similar devices and procedures
  - the event has no temporal relationship with the use of the investigational device or the procedures;
  - the serious event does not follow a known response pattern to the medical device (if the response pattern is previously known) and is biologically implausible;
  - the discontinuation of medical device application or the reduction of the level of activation/exposure - when clinically feasible – and reintroduction of its use (or increase of the level of activation/exposure), do not impact on the serious event;
  - the event involves a body-site or an organ not expected to be affected by the device or procedure;
  - the serious 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);
  - the event does not depend on a false result given by the investigational device used for diagnosis, when applicable;
  - harms to the subject are not clearly due to use error;
  - In order to establish the non-relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the serious event.
- *Unlikely*: The relationship with the use of the device seems not relevant and/or the event can be reasonably explained by another cause, but additional information may be obtained.
- *Possible*: The relationship with the use of the investigational device is weak but cannot be ruled out completely. Alternative causes are also possible (e.g. an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or treatment). Cases were relatedness cannot be assessed or no information has been obtained should also be classified as possible.
- *Probable*: The relationship with the use of the investigational device seems relevant and/or the event cannot reasonably be explained by another cause, but additional information may be

obtained.

- *Causal relationship*: The serious event is associated with the investigational 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 devices and procedures;
  - the event has a temporal relationship with investigational device use/application or procedures;
  - the event involves a body-site or organ that
  - the investigational device or procedures are applied to;
  - the investigational device or procedures have an effect on;
  - the serious 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 serious event (when clinically feasible);
  - other possible causes (e.g. an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or treatment) have been adequately ruled out;
  - harm to the subject is due to error in use;
  - the event depends on a false result given by the investigational device used for diagnosis, when applicable;
- In order to establish the relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the serious event.

Events will be distinguished between the serious adverse events related to the device and those related to the procedures (any procedure specific to the clinical investigation). An adverse event can be related both to procedures and the device. Complications of procedures are considered not related if the said procedures would have been applied to the patients also in the absence of device use/application.

In some particular cases the event may be not adequately assessed because information is insufficient or contradictory and/or the data cannot be verified or supplemented. The sponsor's Medical Monitor and the Investigators will make the maximum effort to define and categorize the event and avoid these situations. Where the Medical Monitor remains uncertain about classifying the serious event, it should not exclude the relatedness and classify the event as "possible".

Adverse Event Outcome Classification

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

- Fatal: If death was possibly, probably, or causally related to the event
- Not recovered / not resolved: Subject has exited the study and the AE is ongoing and not expected to resolve
- Recovered / resolved: The event has fully resolved prior to study exit
- Recovered / resolved with sequelae: The event has resolved prior to study exit, but retained pathological conditions resulting from the prior disease or injury

- Recovering / resolving: The subject has exited the study and the AE is ongoing but expected to resolve
- Unknown: The subject has exited the study and the AE outcome is unknown

Potential Adverse Events and Definitions

Atrial Fibrillation

A disorder characterized by a dysrhythmia without discernible P waves and an irregular ventricular response due to multiple reentry circuits. The rhythm disturbance originates above the ventricles. Degree of severity will be classified according to Common Terminology Criteria for Adverse Events (CTCAE) grade as follows (a semicolon indicates "or" within the description of the grade):

- Grade 1: Asymptomatic, intervention not indicated
- Grade 2: Non-urgent medical intervention indicated
- Grade 3: Symptomatic, urgent intervention indicated; device (e.g., pacemaker); ablation; new onset
- Grade 4: Life-threatening consequences; embolus requiring urgent intervention
- Grade 5: Death

Bronchopleural Fistula

A disorder characterized by an abnormal communication between a bronchus and the pleural cavity. Degree of severity will be classified according to Common Terminology Criteria for Adverse Events (CTCAE) grade as follows (a semicolon indicates "or" within the description of the grade):

- Grade 1: Asymptomatic
- Grade 2: Symptomatic, invasive intervention not indicated
- Grade 3: Hospitalization; invasive intervention indicated
- Grade 4: Life-threatening consequences; urgent intervention indicated
- Grade 5: Death

Bronchopulmonary Hemorrhage

A disorder characterized by bleeding from the bronchial wall and/or lung parenchyma. Degree of severity will be classified according to CTCAE grade as follows (a semicolon indicates "or" within the description of the grade):

- Grade 1: Mild symptoms; intervention not indicated
- Grade 2: Moderate symptoms; medical intervention indicated
- Grade 3: Transfusion, invasive intervention indicated (e.g., hemostasis of bleeding site)
- Grade 4: Life-threatening respiratory or hemodynamic compromise; intubation or urgent intervention indicated
- Grade 5: Death

Burn

Unintended microwave burn – unintended tissue ablation

Unintended microwave burn – vessel thrombosis /thrombus /embolism

Unintended microwave burn – diaphragmatic paresis

A finding of impaired integrity to the anatomic site of an adverse thermal reaction. Burns can be caused by exposure to chemicals, direct heat, electricity, flames and radiation. The extent of damage depends on the length and intensity of exposure and time until provision of treatment. Degree of severity will be classified according to CTCAE grade as follows (a semicolon indicates "or" within the description of the grade):

- Grade 1: Minimal symptoms; intervention not indicated
- Grade 2: Medical intervention; minimal debridement indicated
- Grade 3: Moderate to major debridement or reconstruction indicated
- Grade 4: Life-threatening consequences; hemodynamic compromise
- Grade 5: Death

Cavitation

Seen on follow-up imaging

Death

End of life

Hematoma

A disorder characterized by a localized collection of blood, usually clotted, in an organ, space, or tissue, due to a break in the wall of a blood vessel. Degree of severity will be classified according to CTCAE grade as follows (a semicolon indicates "or" within the description of the grade):

- Grade 1: Mild symptoms; intervention not indicated
- Grade 2: Minimally invasive evacuation or aspiration indicated
- Grade 3: Transfusion; invasive intervention indicated
- Grade 4: Life-threatening consequences; urgent intervention indicated
- Grade 5: Death

Hemolysis

A disorder characterized by laboratory test results that indicate widespread erythrocyte cell membrane destruction. Degree of severity will be classified according to CTCAE grade as follows (a semicolon indicates "or" within the description of the grade):

- Grade 1: Laboratory evidence of hemolysis only (e.g., direct antiglobulin test; DAT; Coombs'; schistocytes; decreased haptoglobin)
- Grade 2: Evidence of hemolysis and >=2 g decrease in hemoglobin
- Grade 3: Transfusion or medical intervention indicated (e.g., steroids)

- Grade 4: Life-threatening consequences; urgent intervention indicated
- Grade 5: Death

Hemoptysis

Coughing up of blood or blood-stained mucous from the lung. Degree of severity will be classified according to CTCAE general guidelines as follows (a semicolon indicates "or" within the description of the grade):

- 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.

Hemothorax

A hemothorax is a type of pleural effusion in which blood accumulates in the pleural cavity. Degree of severity will be classified according to CTCAE general guidelines as follows (a semicolon indicates "or" within the description of the grade):

- 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.

Lung Abscess

Lung abscess is a pus-filled cavity in the lung surrounded by inflamed tissue and caused by an infection. Degree of severity will be classified according to CTCAE general guidelines as follows (a semicolon indicates "or" within the description of the grade):

- 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.

Pleural Effusion

A disorder characterized by an increase in amounts of fluid within the pleural cavity. Symptoms include shortness of breath, cough and marked chest discomfort. Degree of severity will be classified according to CTCAE grade as follows (a semicolon indicates "or" within the description of the grade):

- Grade 1: Asymptomatic; clinical or diagnostic observations only; intervention not indicated
- Grade 2: Symptomatic; intervention indicated (e.g., diuretics or therapeutic thoracentesis)
- Grade 3: Symptomatic with respiratory distress and hypoxia; operative intervention including chest tube or pleurodesis indicated
- Grade 4: Life-threatening respiratory or hemodynamic compromise; intubation or urgent intervention indicated
- Grade 5: Death

Pleural Thickening

Pleural thickening is a descriptive term given to describe any form of thickening involving either the parietal or visceral pleura. Degree of severity will be classified according to CTCAE general guidelines as follows (a semicolon indicates "or" within the description of the grade):

- 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.

Pneumonia

A bacterial, viral, or fungal infection causing inflammation of the lungs. Degree of severity will be classified according to CTCAE grades for Lung Infection as follows (a semicolon indicates "or" within the description of the grade):

- Grade 1: Not applicable
- Grade 2: Moderate symptoms; oral intervention indicated (e.g., antibiotic, antifungal, or antiviral)
- Grade 3: IV antibiotic, antifungal, or antiviral intervention indicated; invasive intervention indicated
- Grade 4: Life-threatening consequences; urgent intervention indicated
- Grade 5: Death

Pneumothorax

A disorder characterized by abnormal presence of air in the pleural cavity resulting in the collapse of the lung. Degree of severity will be classified according to CTCAE grade as follows (a semicolon indicates "or" within the description of the grade):

- Grade 1: Asymptomatic; clinical or diagnostic observations only; intervention not indicated
- Grade 2: Symptomatic; intervention indicated (e.g., tube placement without sclerosis)
- Grade 3: Sclerosis and/or operative intervention indicated; hospitalization indicated
- Grade 4: Life-threatening consequences; urgent intervention indicated
- Grade 5: Death

Post-Ablation Syndrome

A transient, self-limiting symptom/sign complex of low-grade fever, nausea, vomiting, and general malaise. Most patients who experience this syndrome will experience some malaise for 2-7 days, depending on the tumor volume, volume of ablation zone necrosis, and the integrity of the patient's immune system. Degree of severity will be classified according to CTCAE general guidelines as follows (a semicolon indicates "or" within the description of the grade):

- 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.

Post-Procedure Pain

Post-procedure pain will be evaluated both by a Bronchoscopic Ablation Patient Pain and Satisfaction Survey (see Appendix 17.4 of the CIP) and according to the CTCAE general guidelines as follows (a semicolon indicates "or" within the description of the grade):

- 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.

Pulmonary Edema

A disorder characterized by accumulation of fluid in the lung tissues that causes a disturbance of the gas exchange that may lead to respiratory failure. Degree of severity will be classified according to CTCAE grade as follows (a semicolon indicates "or" within the description of the grade):

- Grade 1: Radiologic findings only; minimal dyspnea on exertion
- Grade 2: Moderate dyspnea on exertion; medical intervention indicated; limiting instrumental ADL
- Grade 3: Severe dyspnea or dyspnea at rest; oxygen indicated; limiting self-care ADL
- Grade 4: Life-threatening respiratory compromise; urgent intervention or intubation with ventilatory support indicated
- Grade 5: Death

Pyothorax

An infection in the chest cavity. Degree of severity will be classified according to CTCAE general guidelines as follows (a semicolon indicates "or" within the description of the grade):

- 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.

Ventricular Arrhythmia

A disorder characterized by a dysrhythmia that originates in the ventricles. Degree of severity will be classified according to CTCAE grade as follows (a semicolon indicates "or" within the description of the grade):

- Grade 1: Asymptomatic, intervention not indicated
- Grade 2: Non-urgent medical intervention indicated
- Grade 3: Urgent intervention indicated
- Grade 4: Life-threatening consequences; hemodynamic compromise
- Grade 5: Death

Informed Consent Template	
Clinical Investigation Plan Title	Clinical description of a bronchoscopic approach to ablate lung nodules using the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology
Clinical Investigation Plan Identifier	MDT18010ILSBA
Sponsor/Local Sponsor	Medtronic Minimally Invasive Therapies Group (MITG) Surgical Innovations (SI), Lung Health 161 Cheshire Lane, Suite 100 Plymouth, MN 55441
Principal Investigator:	*Full PI Name (Leave as a placeholder if master study-specific Informed Consent); if not applicable, delete row*
Clinical Site:	*Institution name, address and contact information (Leave as a placeholder if master study-specific Informed Consent); if not applicable, mark as 'N/A' or delete row*
Study Related Telephone:	*Include telephone numbers to be utilized during regular office hours as well as outside regular office hours*
Informed Consent Document Version	Master Consent Template; Version 2; 06Sep19

Confidentiality Statement

INTRODUCTION

In this consent form, "you" always means the study participant.

Why am I being asked to be in this study?

You are being asked to be in a study that involves clinical research. Being in this study is voluntary. Before you decide if you would like to be in the study, it is important you understand why the study is being conducted and what it will involve. Please read this form carefully and ask your doctor if you have any questions. Upon reading this form and asking any questions you have, you will sign and date the last page of this form if you decide to be in this study.

The Emprint™ Ablation Catheter Kit with Thermosphere™ Technology is the device that will be used in your lung ablation procedure. Although this device is approved by regulatory authorities and is commercially available, this procedure is not routinely used in normal clinical care of lung nodules. Only qualified physicians with appropriate training are currently allowed to use it and perform this procedure. If you agree to participating in this study, information will be collected relating to your condition and medical care, including information about your lung ablation procedure.

Study Purpose:

The purpose of this study is to look at the safety and performance of the bronchoscopic ablation procedure using the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology. Detailed medical information will be collected on you and your ablation procedure. You will also be asked to answer questions that are not typically obtained during normal clinical care.

System description:

The device being studied is a microwave ablation system called the "Emprint™ Ablation Catheter Kit with Thermosphere™ Technology". This device uses microwave energy to generate heat that can destroy your lung nodule. The device has thermal-control features to heat up your lung nodule and a small area around your nodule, while avoiding most of your healthy lung tissue. Imaging systems will be used by your doctor to guide the ablation catheter to your lung nodule. You will be given anesthesia for the procedure.

How long will I be in the study? How many people will be in the study?

About 30 will be in this study worldwide. Your participation in the study may last about 1-2 months.
The overall study is expected to last a total of 18 months.

What are my responsibilities during the study?

Being in this study, it is important that you:

- Tell the study doctor about your medical and medication history
- Attend all visits scheduled with the study doctor
- Call the study doctor's office to reschedule a missed visit as soon as possible
- Report any injuries, hospitalizations, emergency room visits, symptoms or complaints to the study doctor or nurse as soon as possible.

What will happen if I am in this study?

Study Procedures:

If you decide to be in this study, the study doctor and study nurse will collect information about you and your medical history. This includes any medication you currently take and any other information in your medical records related to your condition or treatment that may be relevant to your being in the study.

For this study, your study doctor will schedule 2-3 visits with you. You must make sure that you can come to each visit as scheduled.

Baseline Visit
At this visit the following procedures will be carried out:
- Review of eligibility to participate in this study

At this visit the following information will be collected:
- Demographic information (year of birth, gender, etc)
- Medical History such as specific diagnoses, previous lung procedures, smoking history, etc.
- General health information
- Information on your cancerous lung nodule (Review of your computed tomography scan (also called a CT or "CAT" scan)
- Quality of life survey called the EQ-5D *(not typically collected during routine clinical care)*

Procedure Visit
At this visit the following procedures will be carried out:
- Confirmation of eligibility to participate in this study (This is when you will be enrolled in the study)
- The Bronchoscopic Ablation Procedure (This procedure uses a type of X-ray, called fluoroscopy, and Cone Beam Computed Tomography (CBCT) scans, to help guide the doctor during the procedure)
- Images of your lung will be obtained prior to, during, and after the procedure
- Evaluation of your general health

At this visit the following information will be collected:
- Procedure and lung nodule information
- Current medications
- General health information

1-month / Exit Visit
At this visit the following procedures will be carried out:
- Evaluation of your general health
- Follow-up computed tomography scan (also called a CT or "CAT" scan)

At this visit the following information will be collected:
- Current medications
- General health information
- Quality of life survey called the EQ-5D *(not typically collected during routine clinical care)*
- Bronchoscopic Ablation Patient Pain and Satisfaction Survey *(not typically collected during routine clinical care)*

What are the possible risks, side-effects and inconveniences?
The risks of undergoing an ablation procedure are the same whether you choose to take part in the study or not. It is important to understand that you do not need to take part in the study to receive the ablation procedure. Since the Emprint™ Ablation Catheter Kit with Thermosphere™ Technology is commercially available, your doctor will discuss the potential benefits, risks and any alternative options.

Should you wish to take part, you will receive separate consent forms:
- one for the study
- one for the bronchoscopic ablation procedure as part of your standard care

Potential discomforts or complications associated with ablation procedures are listed below. Previous study assessments have shown these complications occur in less than 1% of patients. If you would like more information on these risks, please ask your doctor.

- Post-ablation syndrome (a transient, self-limiting symptom/sign complex of low-grade fever, nausea, vomiting, and general malaise)
- Post-procedure pain (pain because of the procedure)
- Pneumothorax (abnormal presence of air in the chest cavity causing collapse of the lung)
- Hemothorax (bleeding into the chest cavity)
- Pleural effusion (fluid build-up in the cavity)
- Pleural thickening (any form of thickening involving either the parietal or visceral pleura)
- Pulmonary edema (fluid buildup in the lungs themselves which causes difficulty breathing)
- Pneumonia (chest infection)
- Empyema (infection or pus in the chest cavity)
- Lung abscess formation (abscess or collection of pus in the lung)
- Hematoma (a blood clot or bruise)
- Hemoptysis (coughing up of blood or blood-stained mucus)
- Bronchopulmonary hemorrhage (bleeding from the bronchi (windpipes) or lungs)
- Bronchopleural fistula (an abnormal communication between a bronchus and the chest cavity)
- Death (end of life)
- Atrial fibrillation (a dysrhythmia without discernible P waves and an irregular ventricle response to multiple reentry circuits. The rhythm disturbance originates above the ventricles.)
- Ventricular arrhythmia (abnormal heart rate or rhythm)
- Stroke (a decrease or absence of blood supply to the brain resulting in damage to the brain and its functions)
- Damage to other body structures (nerves or vessel damage)
- Hemolysis (laboratory test result that indicate red blood cell destruction)
- Unintended microwave burn (burn in an area that was not meant to be heated)

You may not take part in this study if you are breastfeeding or pregnant. If you are or you become pregnant, there may be risks to you or your unborn child that are not yet known.

There is a possible risk of breach of confidentiality. This risk is minimized by protections described in this document. All records identifying you will be kept confidential and, to the extent permitted by the applicable laws and/or regulations, will not be made publicly available.

Radiation risks:
The CT scan and the imaging that will be carried out as part of your ablation procedure are part of your routine care. If you take part in this study, you will not undergo any additional imaging procedures. These procedures use ionizing radiation to form images of your body and provide your doctor with other clinical information. Ionizing radiation can cause cell damage that may, after many years or decades, turn cancerous. The chances of this happening to you are the same whether you take part in this study or not.

What are the possible benefits of the study?
If you agree to be in this study, it is possible that you may not have any direct medical benefits. Possible benefits in addition to a commercially available product include the following:

- The information from this study may benefit other subjects with lung nodules in the future.
- 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 lung nodules for future patients.

- The information gathered in this study may help doctors to understand how to improve the management of cancer in the lung. It may lead to improvements in care or to the development of new devices/systems/interventions which may benefit yourself or other patients in the future.

What happens when I end being in the study?
Once you have completed the study, your doctor will continue to monitor you as per standard of care.

What other treatment choices do I have if I am not in the study?
You do not have to be in this study to be treated for cancer in your lung.
If you decide not to be in this study, your doctor will discuss with you all the options for medical care, including performing the ablation procedure outside of this study. You may choose no treatment at all. You should discuss other treatments and their possible risks and benefits with your doctor.

Who is paying for this study?
The study site will receive payment from Medtronic for work involved in collecting study data and managing the study at the site. The sponsor will also pay for any additional test or procedures which are not part of your routine care.

Will I be paid for being in this study?
You will not be paid for being in this study.

What will I have to pay for if I am in this study?
Any tests or procedures carried out for study purposes will be provided at no cost to you. Your routine care will be provided by the hospital under standard procedures.

What happens if I am injured or hurt during this study?
Medtronic maintains appropriate clinical trial liability insurance coverage as required under applicable laws and regulations and will comply with applicable local law and custom concerning specific insurance coverage. If required, a Clinical Trial insurance statement/certificate will be provided to your Medical Institution's Ethics Committee.
By agreeing to this, you do not give up any of your legal rights. You do not release the study sponsor, study doctors, or the hospital from responsibility for negligence.

Do I have the right to refuse to be in this study or to leave this study?
Being in this study is voluntary. You may choose not to be in the study or to leave the study at any time for any reason. If you choose not to be in the study, leave the study, or the study is discontinued, this will not result in any penalty and you will not lose any benefits to which you are entitled. Your regular care and your relationship with the hospital or clinic and your doctors will not be affected.

You will be told about any new information that may make you change your mind about staying in the study. You may be asked to sign a new consent form if this occurs.

You may leave the study simply by telling the study doctor. If you choose to leave the study, or the study is discontinued, there are no specific tests that are required prior to leaving the study.

The study doctors may take you out of the study without your permission if:
- It is in your best medical interest
- You are for any reason unable to follow your study doctor's instructions.
- The study sponsor stops the study if:

- It is in the best interest of your health and the health of other study subjects or
- Your study doctor is no longer available to oversee the study and no suitable replacement is found.

If this happens you will be notified about being removed from the study and you will be provided with an explanation about such decision.

Use for countries outside Europe:
All of your health data already collected for the study cannot be removed from the study data and will continue to be used as described in this form even after your participation in the study has ended.
Use for countries in Europe:
All of your health data already collected for the study can still be used by the study sponsor unless you object and ask for deletion of the data.

It is also important to understand that there is a chance your procedure may start, but the ablation portion may not occur if any new information is obtained during the procedure that disqualifies you from having an ablation procedure (for example a risk to your safety is identified). Signing this consent does not automatically enroll you into the study. If you do sign this consent and don't undergo the ablation procedure, the reason you could not be enrolled will be recorded.

What is the role of the sponsor's representative?
Trained Medtronic personnel may be present at the bronchoscopic procedure and at study follow-up visits. The role of the Medtronic person is to give technical support. Authorized sponsor representatives will also check data for accuracy and regulatory purposes.

How will the sponsor use the study information?
If you decide to participate in the study, Medtronic (including, for purposes of this section, its agents and contractors) and others who work with the study will see health information about you. This consent form governs how your health information is disclosed and used.

This consent form describes the study, and what Medtronic will do with the study data, including your health information received during the study. Medtronic will keep your health information confidential in accordance with all applicable laws and regulations. Medtronic may use your health information to conduct this research, as well as for additional purposes, such as overseeing and improving the performance of its device, new medical research and proposals for developing new medical products or procedures. Any reports or publications about the study or any other research will not include your name or a description of you. Information received during the study will not be used to market to you; your name will not be placed on any mailing lists or sold to anyone for marketing purposes. Regulations and applicable laws, control Medtronic's work in developing and assuring the safety and quality performance of its medical devices. Medtronic may disclose your health information to U.S. and foreign government authorities responsible for assuring the safety of medical devices. Medtronic also may disclose your health information to Ethics Committees and other persons who are required to watch over the safety and effectiveness of medical products and therapies and the conduct of research. You agree to allow Medtronic to use study data in these ways. You also agree to allow governmental authorities to inspect your health information.

To participate in the study, you will need to sign this consent form.

Where can I find out about the study results?
A description of this study will be available on http://www.ClinicalTrials.gov. This website will not include information that can identify you. At most, the website (databases) will include a summary of the

results. You can consult the general outcome and results of this study after they have been made publicly available by consulting this website.

Who can I call with questions, complaints or if I'm concerned about my rights as a participant?

If you have any questions about the research or being in this study, you should contact *insert name* at *insert telephone number.*

If you think you have a research-related injury, you should contact *insert name* at *insert telephone number.*

If you have any questions about your rights as a participant you should contact *insert name* at *insert telephone number.*

Who has reviewed the study?

This study was reviewed and approved by the *insert name of committee* Research Ethics Committee.

INFORMED CONSENT FOR THE MEDTRONIC NAVABLATE CLINICAL STUDY
SUBJECT INFORMED CONSENT FORM SIGNATURE SHEET

- I have read the subject information for this study and my study doctor has answered all my questions regarding the study.
- I had sufficient time to consider my participation in this study, I am aware that participation in this study is completely voluntary, and I agree to follow the instructions from the study doctor.
- I realize that I may decide to refuse participation or stop participation at any time without penalty and without affecting the quality of my health care or the relationship with my study doctor.
- I understand and agree that personal information about me will be collected from my medical records, used and processed (manually and by computer) by the manufacturer of a product used in my treatment or any other designated party that is involved in the study (e.g., hospital, study doctor, regulatory authorities, ethics committees).
- I understand and agree that representatives from Medtronic, regulatory authorities and the Ethics Committee will be granted direct access to my medical records.
- I understand and agree that the study doctor(s)/hospital will release the relevant personal information about me for the purpose of the study.
- I understand that I am entitled to access the personal information collected about me and to have inaccuracies corrected.
- I agree to voluntarily be in and comply with this study.
- I understand that I will receive a dated and signed copy of the subject informed consent form.

It is your choice if you would like your personal physician to be informed of your participation in this study. Please check one of the boxes below to show your choice:

! must be checked by subject

☐ I agree to inform my personal doctor about my participation in this study

☐ I do not agree to inform my personal physician about my participation in the study

Signature of the subject

I agree to be in this study and I have consented before the initiation of any study specific procedures.

Subject:

Name	Signature	Date (DD/MMM/YYYY)
	Must be written by subject!	*Must be written by subject!*

Study doctor or designated person by study doctor:
I have conducted the informed consent discussion.

Name	Signature	Date (DD/MMM/YYYY)
	Must be written by study doctor or delegate!	*Must be written by study doctor or delegate!*

DOCUMENT CHANGE HISTORY

Revision	Description of Change	Author
1.0	08-May-2018 First issue	Jennifer Wolvers
2.0	06-Sep-2019. Updated to be MDR compliant. Updates to this sample ICF were also made based on comments/suggestions from country specific sites.	Jennifer Wolvers