Instruction for Use: Cryoprobe

Before using the IceCure Cryoablation system with its accessories you must read and fully understand the IceCure Cryoablation system User Manual (for IceSense3® or ProSense™). While this document is designed to provide instructions in the use of the **cryoprobe** with IceCure Cryoablation system, it is not intended to take the place of the User Manual and of the user training course which must be completed before using the system.

Intended use of IceCure Cryoablation System (IceSense3® or ProSense™)

ProSense™ cryoablation system is intended for cryogenic destruction of tissue during surgical procedures by the application of extreme cold temperatures. The ProSense™ cryoablation system is indicated for use as a cryosurgical tool in the fields of general surgery (including breast and liver tissue), dermatology, thoracic surgery (including lung tissue), gynecology, oncology (including Muskuloskeletal tissue), proctology, and urology (including kidney tissue). The ProSense™ cryoablation system may be used with an ultrasound device to provide real-time visualization of the cryosurgical procedure.

This cryotherapy should only be executed if the operative standard therapy and established therapies cannot be applied.

Indications for Use

ProSense™ cryoablation system is intended for cryogenic destruction of tissue during surgical procedures by the application of extreme cold temperatures. The ProSense™ cryoablation system is indicated for use as a cryosurgical tool in the fields of general surgery (including breast and liver tissue), dermatology, thoracic surgery (including lung tissue), gynecology, oncology (including Musculoskeletal tissue), proctology, and urology (including kidney tissue). The ProSense™ cryoablation system may be used with an ultrasound device to provide real-time visualization of the cryosurgical procedure.

Urology: The system may be used to ablate prostatic tissue. The system may be used to ablate kidney tissue including renal cell carcinoma. The system may be used for the ablation of prostate tissue in cases of prostate cancer and benign prostatic hyperplasia.

Oncology: The system may be used for ablation of cancerous or malignant tissue. The system may be used for ablation of benign and malignant breast tumors. The system may be used for ablation of benign and malignant lung tumors. The system may be used for ablation of benign and malignant musculoskeletal tumors. The system may be used for ablation of benign and malignant liver tumors. The system may be used for ablation of benign tumors. The system may be used for palliative intervention.

Dermatology: The system may be used for the ablation or freezing of skin cancers and other cutaneous disorders.

Gynecology: The system may be used for the ablation of malignant neoplasia or benign dysplasia of the female genitalia.

General Surgery: The system may be used for the ablation of leukoplakia of mouth, angiomas, sebaceous hyperplasia, basal cell tumors of the eyelid or canthus area, ulcerated basal cell tumors, dermatofibromas, small hemangiomas, mucocele cysts, multiple warts, plantar warts, hemorrhoids, anal fissures, perianal condylomata, pilonidal cysts actinic and seborrheic keratoses, cavernous hemangiomas, recurrent cancerous lesions. The system may be used for the destruction of warts or lesions. The system may be used for the palliation of tumors of the oral cavity, rectum, and skin. The system may be used for ablation of breast fibroadenomas and breast tumors.

Thoracic Surgery: The system may be used for the ablation of arrhythmic cardiac tissue. The system may be used for the ablation of cancerous lesions, including lung tissue.

Proctology: The system may be used for the ablation of benign or malignant growths of the anus and rectum. The system may be used for the ablation of hemorrhoids.

This cryotherapy should only be executed if the operative standard therapy and established therapies cannot be applied.

Clinical decisions

Practitioners are solely responsible for all clinical use of the IceCure cryoablation system and for any results obtained with the device.

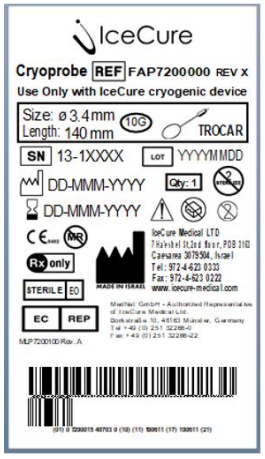

Figure 1: Single use cryoprobe label

A number of harmonized symbols relating to safety requirements and standards are found on the cryoprobe label. These symbols are listed in the IceCure cryoablation system User Manual.

Cryoprobes are not compatible with magnetic resonance imaging

Cryoprobe Selection

Cryoprobes are fragile and can be damaged if mishandled. Do not use a cryoprobe that has been bent, dropped, hit against a hard surface or compromised in any manner, as damage to the cryoprobe may have occurred.

The cryoprobe tip must be covered when not within the target tissue.

Prior to starting a procedure, select a cryoprobe according to your clinical judgment.

Table 1: Cryoprobe selection

Cryoprobe Diameter/ Gauge	Shaft Length + Tip ±3mm	Tip Shape	Ice Ball Shape	Cool Zone Center From needle tip [mm]	Part Number
3.4 mm / 10G	127 mm	Trocar	Spheric	12 mm	FAP7100000
3.4 mm / 10G	140 mm	Trocar	Elliptic	20 mm	FAP7200000
3.4 mm / 10G	185 mm	Pencil	Elliptic	20 mm	FAP7400000
3.4 mm / 10G	185 mm	Trocar	Elliptic	20 mm	FAP7410000
2.4 mm / 13G	124 mm	Trocar	Spheric	10 mm	FAP7600000
2.4 mm / 13G	134 mm	Trocar	Elliptic	14.5 mm	FAP7800000

Cryoprobes of 185 mm length are intended for penetrating and freezing soft tissue and can be used in laparoscopic procedures, while shorter cryoprobes are typically used for percutaneous procedures under reduced mechanical stress. It is preferred to use the adapted lengths according to the superficiality of the lesions. Select the cryoprobe based on ice ball size you want to obtain the cooling zone location as defined in the table above.

Figure 2: For illustration only Color Tag labels for cryoprobe and the matching introducer

The cryoprobe serial number (S/N) appears on the screen/cryoprobe package/cryoprobe plastic grip.

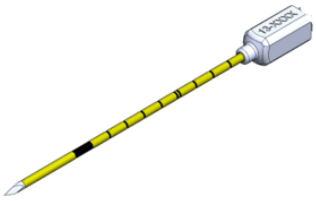

Figure 3: The Cryoprobe

Cryoprobe connection

Cryoprobes are single-use devices supplied in single use sterile packaging.
Reuse of single-use devices affects their performance and can cause cross-contamination.

Connect the cryoprobe to the cryohandle, while maintaining sterility of the cryoprobe:
1- Remove the plug that covers the cryoprobe connection point.
2- Insert the cryoprobe into the insertion point in the handle as shown on the system screen and screw it until a “NEXT” button appears on screen then confirm screwing by an additional slight rotation to confirm that cryoprobe connection is secured.
3- Remove the cryoprobe tip protector.

When done, press **Next** on the screen.

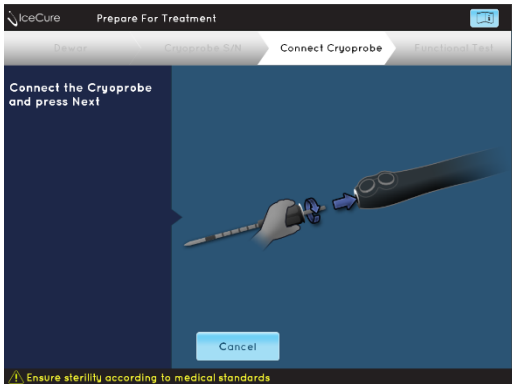

Figure 4: Cryoprobe connection screen

Cryoprobe operation

Perform a functional **pre-test** to ensure system efficacy and safety as explained in the User Manual.
If a functional problem occurs or there is any unusual appearance (such as frost on the plastic cover near the cryohandle, bubbles or any unusual appearance), press **Cancel** on the system screen and follow system instructions until you are required to safely remove the cryoprobe from the cryohandle. Before operating the cryoablation system, make sure you have completed all pre-operational stages.

Do not start the Freeze step before the cryoprobe cool zone center is aligned with the center of the target tissue.

Before activating the freeze step, insert the cryoprobe into the target tissue under imaging guidance, and follow these steps:

1. Confirm longest dimension of the target tissue
2. Plan the trajectory of the cryoprobe prior to placement. When clinically safe, the center of the cool zone shall be along the longest dimension of the target tissue.
3. The black safety mark should be completely in the tissue.
4. In percutaneous approach, perform a 3 mm skin incision (for example using #11 blade) before the cryoprobe is inserted.
5. Position the tip of the cryoprobe at the distal end of the long axis of the target tissue, when clinically safe
6. Center of the cool zone, should be in the center of the tissue to be ablated (see figure 2 for the distance of the cool zone from the tip of the cryoprobe that is visible under Ultrasound imaging).
7. Maintain sterility and patient safety.

Be aware of the markings on the cryoprobe: the **wide black mark** closest to the tip is the safety mark. In percutaneous procedures **it must be completely inside the tissue** to avoid skin burns. The rest of the marks indicate depth of cryoprobe insertion: each mark equals one centimeter with distinctive markings at 5 and 10 cm (50 & 100 mm).

Figure 5: Illustration of FAP7200000 cryoprobe markings

Once you have verified that the cool zone center of the cryoprobe is located in the center of the target tissue, you may begin freezing.

Portions of the cryoprobe other than the freeze zone, including the plastic cover that is located near the cryohandle, may become cold and cause tissue damage. If unwanted freezing occurs, immediately stop the freeze step. In case of frost on shaft, start Extraction if possible. If not, wait for passive Thaw. In both cases, use skin protection techniques.

To prevent injury, ice ball growth must be monitored under imaging guidance.
During **Thaw**, the ice ball melts partially or totally depending on the thaw time and the tissue properties.
Keep the cryoprobe location steady in the target tissue during all of the thaw period. Control the process under Ultrasound or other imaging system.
The **Extraction** step occurs at the end of every treatment. Its purpose is to allow the cryoprobe’s removal from the target tissue in the fastest and safest way.
At the end of the extraction step, a message will be displayed on system screen. Wait for the message, then gently remove the cryoprobe from the target tissue.
If the cryoprobe cannot easily be extracted from the tissue, press **Extraction** on screen to initiate another Extraction step.
In case the Extraction process isn’t available, wait for passive Thaw.

After the Extraction step, before extracting the cryoprobe, make sure that the cryoprobe can be easily removed from the tissue.

Do not force removal of the cryoprobe from the tissue as it might increase the risk of tissue damage. Continue the Extraction step or wait for passive thaw until the cryoprobe can be withdrawn easily.

Cryoprobe disengagement

After removing the cryoprobe from the target tissue, and only if system screen displays a message that it is safe to disengage the cryoprobe, detach the cryoprobe from the cryohandle as follows:

1. Unscrew the used cryoprobe from the cryohandle and dispose of it appropriately.
2. Remove the single-use sterile cover from the cryohandle.
3. Close the cryohandle with the covering plug.

Following each cryoablation procedure, discard the single use devices (single-use cryoprobe, single-use temperature sensor, cryohandle, flexible hose and touch screen covers and sleeves).
All single use devices are considered to be medical waste and must be disposed of in accordance with medical waste laws and hospital standards. Sharp objects such as the cryoprobe, introducer and temperature sensor must be disposed of in a sharps waste container.

Contraindications

Severe infection, uncorrectable coagulopathy, hemodynamic or respiratory instability.

Predictable Adverse Events

General surgery/ Minimal Invasive Procedures - Mild/moderate adverse events: infection, bleeding, pain, fever, thermal injury, injury to adjacent organs, pneumonia, fall, internal adhesions, incomplete treatment changes in the laboratory parameters-elevation in aspartate aminotransferase and/ or alanine aminotransferase level (this reflects hepatocellular damage), minimal self-limited serum bilirubin level elevation, hemorrhage, hematoma, myoglobinemia, pleural effusion, hemothorax, pneumothorax, thrombosis, diarrhea, nausea, deep vein thrombosis (DVT), transient ischemic attack, hypertension, hypothermia, treatment site reaction, local neuropathy, frostbite, skin burn, vagal reaction, vomiting, needle seeding, user accidental injury. **Severe adverse events**: infection, thermal injury, procedure done on the wrong patient/ part of the body, retention of foreign object after surgery, pulmonary emboli, congestive heart failure, stroke, fall, severe changes in the laboratory parameters-elevation in aspartate aminotransferase and/ or alanine aminotransferase (this reflects hepatocellular damage), life threatening serum bilirubin level elevation, perirenal fluid collection, hemorrhage, cryoshock (hypotension), respiratory compromise, multi organ failure, disseminated intravascular coagulation (DIC), abscess, pleural effusion, hemothorax, pneumothorax, thrombosis of the portal vein branches, allergic/anaphylactoid reaction, angina/coronary ischemia, myocardial infarction, arrhythmia, atelectasis, adjacent organ injury.

Anesthesia Mild/moderate adverse events: hypoxia, hypotension -low blood pressure, cough, residual neuromuscular block in recovery, intubation complications, slow to regain consciousness, anesthetic turn off too early.

Anesthesia Severe adverse events: hypoxia, hypotension – low blood pressure, residual neuromuscular block in recovery.

Cryoablation procedure in general - Mild/moderate adverse events: hematoma, hemorrhage, infection, pain, fever, thermal injury, thrombocytopenia, coagulation dysfunction. **Severe adverse events:** haemorrhage, infection, tumor seeding, thermal injury, thrombocytopenia, coagulation dysfunction, parenchymal or cryoablated organ injury, incorrect interpretation of post-cryo changes, intra vessels / intra bone gas, emboli, myocardial infarction.

Percutaneous ablation procedure - Mild/moderate adverse events: percutaneous hematoma and bleeding infection, adjacent organ injury, CT related adverse effects: radiation, elevated creatinine and renal function injury, reaction. **Severe adverse events:** percutaneous bleeding, infection, adjacent organ injury, **CT related adverse effects:** radiation, acute renal injury, anaphylactic shock in reaction to contrast agent admission, gas emboli.

Laparoscopic procedure - Mild/moderate adverse events: vascular and visceral injury, general anesthesia related AE, pneumoperitoneum (that can cause hemodynamic alterations), post procedural abdominal adhesions, abdominal wall hematoma, wound infection and fascial injury. **Severe adverse events:** vascular and visceral injury, general anesthesia related AE, port site metastasis, pneumoperitoneum (that can cause hemodynamic alterations), post procedural abdominal adhesions, cryoprobe and trocar insertion include injuries to major retroperitoneal vessels and to bowel, abdominal wall hematoma, fascial dehiscence and herniation, umbilical hernia, and umbilical wound infection.

Breast - Fibroadenoma and breast cancer: **Mild/ moderate adverse events**: bleeding from breast puncture site, local breast hematoma, local breast infection and thermal injury to the breast skin, breast skin bruising, breast swelling, ecchymosis, edema, fat necrosis. **Severe adverse events**: thermal injury.

Urology - **Renal and Prostate: Mild/moderate adverse events**: adjacent organ injury, allergic reaction, bleeding, DVT, cystitis , Hematuria, hypotension, Idiosyncratic reaction, ileus, infection, pleural effusion, pneumothorax, probe site paresthesia, mild renal failure, renal infract, voiding dysfunction, urinary tract obstruction, hematomas, ejaculatory dysfunction, erectile dysfunction, penile paresthesia, pelvic pain, perineal pain. **Severe adverse events:** abscess, adjacent organ injury, renal artery/renal vein injury, anaphylactic reaction, coronary ischemia, myocardial infraction, bleeding, death, DVT, hypotension, pulmonary embolism, severe renal failure, stroke, Idiosyncratic reaction, ileus, infection lumbar radiculopathy, pelvic vein thrombosis, pleural effusion, pneumothorax, renal hemorrhage , severe urinary tract obstruction, renal vein thrombosis, rectourethral fistula, scrotal edema, ureteral stricture, renal infract, sepsis, urinary tract leak, urethral sloughing, urethral stricture, urinary fistula, urinary frequency/urgency, urinary incontinence, urinary retention, bladder neck contracture, stroke, need for transfusion due to hemorrhage, tumor seeding, gastro intestinal tract injury.

Thoracic surgery - Lung and cardiac arrhythmia: Mild/moderate adverse events: frostbite, respiratory failure, pneumothorax, Hemothorax, pleural effusion, pneumonia, empyema, hemoptysis, lung collapse, thrombosis, phrenic nerve palsy, Pain, fever, cough, back pain, skin injury, pulmonary emboli, Loss of speech (temporary aphasia from laryngeal nerve damage), arm paresis, burn, hemorrhage, pneumonitis. **Severe adverse events:** respiratory failure/arrest, pneumothorax, hemothorax, pleural effusion, pneumonia, empyema, lung collapse, thrombosis, phrenic nerve palsy, subcutaneous emphysema, death due to Acute respiratory distress syndrome, pulmonary emboli, prolonged chest tube drainage, prolonged intubation pulmonary insufficiency/failure, hemorrhage, dyspnea, atelectasis.

Liver - Mild/moderate adverse events: changes in the laboratory parameters-elevation in AST (Aspartate Aminotransferase) and/ or ALN (Alanine aminotransferase) level - reflects hepatocellular damage of normal liver parenchyma, minimal self- limited serum bilirubin level elevation, hematoma, hemorrhage, nyoglobinemia, pleural effusion, hemothorax, pneumothorax, thrombosis. **Severe adverse events**: Severe changes in the laboratory parameters-

elevation in AST (aspartate aminotransferase) and/ or ALN (Alanine aminotransferase) level - reflects hepatocellular damage of normal liver parenchyma, life threatening serum bilirubin level elevation, hemorrhage, cryoshock (hypotension, respiratory compromise, multi organ failure, DIC), post procedural abscess- due to conduit ascending bacterial (especially in patients with history of biliary interventions and biliary enteric anastomosis), pleural effusion, hemothorax, pneumothorax, thrombosis of the portal vein branches.

Musculoskeletal - Mild/moderate adverse events: muscular injury, pain, swelling, osteonecrosis, osteomyelitis, chondrolysis, nerve palsy, motor dysfunction, peri-ablational neuropathies. **Severe adverse events:** compartment syndrome osteonecrosis, osteomyelitis, chondrolysis, nerve palsy, motor dysfunction, peri-ablational neuropathies, bowel damage, urinary tract damage, pericardial effusion in (in chest wall ablations), avascular necrosis of femur head, ureteral stricture.

Gynecology - Mild/ moderate adverse events: spotting, urinary tract infection, treatment site infection, uterine bleeding, genitourinary perforation, pelvic pain.

Dermatology - Mild/ moderate adverse events: skin burn/frostbite, wound complication and wound infection.

General predictable adverse events when using the introducers: Trauma to tissue, incomplete treatment, infection, user accidental injury, needle seeding.

Cryoprobe technical specifications

The packed cryoprobes shall be stored in a dry, cool, well-ventilated and clean environment without corrosive gas.

In general, IceCure's Cryoprobes are available in various diameters (2.4 mm and 3.4 mm), various ice ball shapes (Spheric, Ellipsoid), various tips (trocar, blunt and pencil) and various lengths (124mm to 185 mm external shaft length) according to the expected application, treated tumor size and surgery approach.

The opening of the cryoprobe pouch should be where the “PEEL HERE” label is positioned.

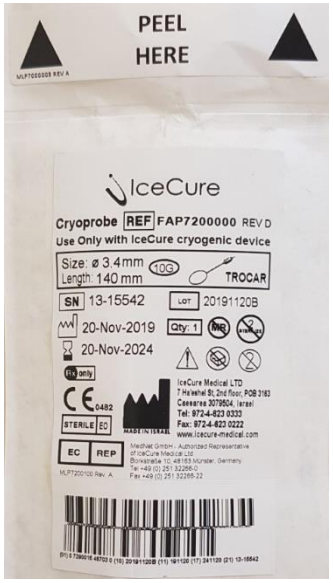

Figure 6: “Peel Here” label

Ref number: FAP 7100000, FAP 7200000, FAP 7400000, FAP 7410000, FAP 7600000, FAP 78000000.

* Certain configurations are not available in some regions.

Temperature Range: -196° C to +40° C
Needle diameter: 2.4 mm (13G) or 3.4 mm (10G)

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