iovera°®

System User Guide

Legal Notice

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

Information in this document is subject to change without notice.

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Patents

For information on patents and patents pending go to: https://www.ioverapro.com/company/patents.

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Chapter 1 – Safety

Introduction

Carefully read all instructions prior to using the iovera° system. Observe all contraindications, warnings, and cautions noted in this chapter and throughout the guide. Failure to do so may result in the possibility of injury to the patient or the operator, inferior treatment outcomes, or damage to the device.

iovera° System Warnings and Cautions

The following symbols and descriptions are found at appropriate places throughout this document:

WARNING!	**This symbol indicates a hazardous situation which, if not avoided, could result in patient or user injury.**
CAUTION!	This symbol indicates a hazardous situation, which, if not avoided, could result in equipment damage or malfunction.

NOTICE	This symbol is to provide information that helps to maintain the highest iovera° system performance.

General Warnings

Warning	Description
Electrical	The iovera° system may be hazardous if misused. Only connect the device to a proper mains power outlet and use only the Electrical Adapter supplied by Pacira Pharmaceuticals, Inc. There are no user-serviceable parts in or on the iovera° system. The effects of interference from radio frequency identification (RFID) readers have not been studied on the iovera° system. The iovera° system is not recommended for use in close proximity to RFID readers. The iovera° system is not intended for use in a Magnetic Resonance Environment. The iovera° system needs special precautions regarding electromagnetic compatibility (EMC) and needs to be installed and put into service according to the EMC information provided in this manual. Portable and mobile radiofrequency (RF) communications equipment can affect the iovera° system. The use of accessories other than those specified by Pacira Pharmaceuticals, Inc. may result in increased EMISSIONS or decreased IMMUNITY of the iovera° system, resulting in improper operation. The iovera° system should not be used adjacent to or stacked with other equipment. If adjacent or stacked use is necessary, the iovera° system should be observed to verify normal operation in the configuration in which it will be used. Operation of this equipment in environments not complying with the conditions specified in Appendix A may result in improper operation (e.g., excessive temperature in the skin warmer or excessive pressure in the Cartridge). In the rare event that a cooling cycle fails to stop, you must immediately fully vent the remaining cryogen in the Cartridge or disengage the Smart Tip from the Handpiece. The Data Port is not for customer use. Do not remove the cover or connect a USB cable. Do not touch any part of the Data Port and a patient simultaneously. The iovera° system is not intended for use in an oxygen rich environment (≥ 25%). **Danger: Explosion Hazard. Do Not Use in Presence of Flammable Anesthetics.**
iovera° System Components	The iovera° system is intended for use only with the provided components. Substituting different components (Cartridge, Smart Tip, Electrical Adapter for the Charging Dock) for those supplied by Pacira Pharmaceuticals, Inc. may damage the device and/or create a hazard to the patient or the operator.

General Warnings continued

Warning	Description
Compatible 3rd Party Nerve Stimulators	The following 3rd Party nerve stimulators have been tested for compatibility with the Smart Tips with a STIM designation: • B Braun Stimuplex HNS 12 • Xavant Stimpod NMS 410
Nitrous Oxide	Nitrous oxide is an oxidizing agent that may accelerate combustion. DO NOT store Cartridges near flammable materials or igniters. Store only where temperatures do not exceed 50 °C (122 °F). Nitrous oxide is under high pressure. A venting Cartridge may dislodge with high force if removed from the Handpiece. Allow system to depressurize completely before attempting to remove the Cartridge from the device. Store away from heat source. Keep away from sunlight. Exercise caution when removing the Cartridge as it may be very cold. Do not inhale Nitrous oxide and use in a well-ventilated area.
iovera° Smart Tip	The iovera° Smart Tip houses the closed-end needle or needle array used to deliver the treatment. The iovera° system generates freezing temperatures that result in tissue destruction. The ends of the iovera° Smart Tip needles will reach subzero temperatures and could damage exposed tissues. Do not use an expired iovera° Smart Tip. Check the sterile package for expiration date. Carefully inspect the iovera° Smart Tip package prior to use for any breach of the sterile barrier or damage to the contents. If the sterile barrier integrity is compromised or the contents are damaged, DO NOT USE and contact a Pacira Pharmaceuticals, Inc. representative. The iovera° Smart Tip is sterile. Touching the iovera° Smart Tip needles may compromise sterility. The iovera° Smart Tip comes protected in the Smart Tip Cap. DO NOT remove the Smart Tip Cap until the system is ready to perform a cycle. The iovera° Smart Tip is single-use. Do not reuse, reprocess or re-sterilize.
Treatment	Care should be taken when selecting the target treatment site. Treatment outside the intended target area could result in loss of motor function or unintended freezing of surrounding structures. Minimize any movement of the Handpiece once the Smart Tip is in place and the cooling cycle has started. Excessive movement with the Smart Tip in place could result in damage to subcutaneous tissue. Do not re-treat the same area immediately after a successful treatment cycle. Allow the skin to rewarm first to reduce the risk of skin injury. As applicable, ensure that the STT2309 Smart Tip needles are fully inserted into the skin so that the skin warming feature is touching the skin. Failure to fully insert the STT2309 Smart Tip may result in skin injury. See supplemental instructions for use in Appendix C for details. Do not reposition or remove the Smart Tip if resistance is felt. This may indicate the cooling zone is still attached to the Smart Tip and moving the Smart Tip may result in damage to subcutaneous tissue. Do not attempt to remove the Smart Tip from the patient while cooling is in process. Doing so could result in damage to subcutaneous tissue. However, if the RF Cannula Introducer is utilized, the iovera° Smart Tip can be removed from the cannula once the treatment cycle has completed. Nevertheless, the introducer should be kept in place until no resistance is felt upon its removal, Appendix F.

General Cautions

Caution	Description
iovera° System	Carefully read all instructions prior to using the iovera° system. Observe all contraindications, warnings and cautions noted in this chapter and throughout this guide. Failure to do so may result in the possibility of injury to the patient or the operator, subpar treatment outcomes, or damage to the device. Never submerge the iovera° Handpiece or the Charging Dock into any liquids. Do not allow liquids or particulates into the Cartridge chamber. Doing so could block nitrous oxide flow and prevent or limit cooling.

Symbols

The following symbols are associated with the iovera° system:

Symbol	Description
CE 0344	This marking on a product is a manufacturer's declaration that the product complies with the essential requirements of the relevant European health, safety, and environmental protection legislation.
MD	Medical Device
	For Single Use Only, Do Not Reuse
STERILE EO	Sterilized Using Ethylene Oxide — The iovera° Smart Tip is sterilized
	Do no Re-Sterilize
LOT	Lot Number
SN	Serial Number
REF	Catalog Number
	Contains electronics — Dispose according to local regulations or return to Pacira Pharmaceuticals, Inc.
5V⎓/2.4A	5 Volt Direct Current, 2.4 Amps, cylindrical connector with positive center
	User must follow Instructions for Use (this guide)
	Use By Date
	Storage Temperature Limitation
	Date of Manufacture
	Legal Manufacturer
	Caution — Refer to manual for important safety information
	Warning — Refer to manual for important safety information
	Keep Away from Sunlight
	Keep Dry
	Do Not Use if Package is Damaged

Symbol	Description
	Type BF Applied Part (designation for medical devices that come into contact with a patient)
	iovera° Smart Tip
	RF Transmitter
	MR Unsafe; Product is unsafe for use in a magnetic resonance environment
	Must wear protective gloves
	Warning — low temperatures/freezing conditions
	The product is intended for use by, or under the direction of, a physician
	Identifies the range of temperature to which the product can be safely exposed during transit and storage; The upper and lower temperature limits are shown adjacent to the upper and lower horizontal lines
	Identifies range of atmospheric pressure to which the product can be safely exposed during transit and storage; The upper and lower atmospheric pressure limits are shown adjacent to the upper and lower horizontal lines
	Identifies range of relative humidity to which the product can be safely exposed during transit and storage; The upper and lower relative humidity limits are shown adjacent to the upper and lower horizontal lines

Indications for Use

The iovera° system is used to destroy tissue during surgical procedures by applying freezing cold. It can also be used to produce lesions in peripheral nervous tissue by the application of cold to the selected site for the blocking of pain. It is also indicated for the relief of pain and symptoms associated with osteoarthritis of the knee for up to 90 days. The iovera° system is not indicated for treatment of central nervous system tissue.

When stimulation compatible components are used, the iovera° System can also facilitate target nerve location by conducting electrical nerve stimulation from a compatible 3rd party nerve stimulator.

Intended User

The iovera° system is intended for use by, or under the direction of, a physician.

Target Population

The iovera system is used for the relief of pain and symptoms associated with musculoskeletal, soft tissue and neuromuscular disorders where peripheral nerves can be accessed. Cryoneurolysis with the iovera° system has not been associated with secondary neuritis or neuroma formation in prior clinical experience, and there is no evidence that repeat cryoneurolysis treatments cause long-term changes to nerve function or structure[1,2].

Important Safety Information

Contraindications

The iovera° system is contraindicated for use in patients with the following:

- Cryoglobulinemia, paroxysmal cold hemoglobinuria, cold urticaria, Raynaud's disease, and open and/or infected wounds at or near the treatment site

Potential Complications

As with any surgical treatment that uses needle-based therapy and local anesthesia, there is a potential for site- specific reactions, including, but not limited to:

- Ecchymosis, edema, erythema, local pain and/or tenderness, and localized dysesthesia

Proper use of the device as described in the User Guide can help reduce or prevent the following complications:

- At the treatment site(s): injury or skin lesions related to the application of cold or heat.
- Outside the treatment site(s): loss of motor function

[1] Ilfeld BM, Preciado J, Trescot AM. Novel cryoneurolysis device for the treatment of sensory and motor peripheral nerves. *Expert Rev Med Devices*. 2016 Aug;13(8):713-25.

[2] Hsu M, Stevenson FF. Wallerian degeneration and recovery of motor nerves after multiple focused cold therapies. *Muscle Nerve*. 2015; 51(2):268-275.

Clinical Study, Osteoarthritis of the Knee[3]

A multi-center, prospective, randomized, double-blind, sham-treatment controlled trial enrolling 180 subjects was conducted in subjects diagnosed with Grade II or III osteoarthritis of the knee (Kellgren-Lawrence classification grading scale) and washed out of all pain medication. A local anesthetic was used to create a diagnostic block of the infrapatellar branch of the saphenous nerve, as assessed by a 50% decrease in VAS pain upon standing from a seated position or walking upstairs, to confirm that the subject was a candidate for treatment.

121 subjects were treated with the iovera° system and 59 subjects were treated with a sham device, with ages ranging from 36 to 75 years. Data from all 180 subjects enrolled were collected and analyzed. The primary endpoint (superiority of the iovera° treatment over sham treatment for reducing pain and symptoms due to osteoarthritis in the knee as assessed by the Total Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scale from baseline to Day 30) was met, p=0.001, see Table 1 below. Subjects treated with the iovera° system reported substantially more pain and symptom relief as subjects treated with the sham device (55% improvement versus 33% improvement, respectively).

Secondary endpoints were also met, including statistically significant superiority of iovera° treatment over sham treatment for relief of pain and symptoms due to osteoarthritis of the knee on the Total WOMAC scale (pain, stiffness, function) at Day 60 and a statistically significant number of patients reported clinically significant pain relief (30% reduction in WOMAC pain score) through 90 days after treatment with the iovera° system, as shown in Table 1 below.

Table 1

		iovera° treatment group (n=121)	Sham control group (n=59)
Reduction in pain and symptoms on Total WOMAC scale 30 days post-treatment		-73.31[1]	-42.18
Percentage of patients reporting 30% improvement in pain and symptoms on Total WOMAC scale post-treatment	30 days 60 days 90 days	74.58% 76.79% 80.18%	44.83% 56.90% 54.39%

LS Means and p-value were obtained by fitting an ANCOVA model with treatment as factor and WOMAC baseline score as a covariate.

There were no serious device-related or procedure-related adverse events. All device-related adverse events were as anticipated per the device labeling. A summary of adverse reactions, including site-specific reactions and/or known effects from cryoanalgesia that lasted longer than 30 days follows.

Table 2

Adverse Reaction	iovera° (n=121)	Sham (n=59)
Numbness	18 (14.8%)	1 (1.7%)
Tenderness upon palpitation	14 (11.6%)	8 (13.6%)
Local pain	8 (6.6%)	4 (6.8%)
Altered sensation/localized dysesthesia	3 (2.5%)	2 (3.4%)
Tingling	3 (2.5%)	1 (1.7%)
Swelling	3 (2.5%)	3 (5.1%)
Bruising	3 (2.5%)	2 (3.4%)
Itching	2 (1.6%)	0
Vasovagal response	1 (0.8%)	0
Knee pain	1 (0.8%)	2 (3.4%)
Redness/inflammation	1 (0.8%)	1 (1.7%)
Pain, aggravated	0	1 (1.7%)

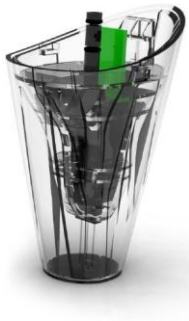
100% of subjects were subjected to a diagnostic lidocaine block to ensure that patients with an appropriate evaluation were enrolled in the study.

[1] Ilfeld BM, Preciado J, Trescot AM. Novel cryoneurolysis device for the treatment of sensory and motor peripheral nerves. *Expert Rev Med Devices*. 2016 Aug;13(8):713-25.

3 Radnovich R, Scott D, Patel AT, et al. Cryoneurolysis to treat the pain and symptoms of knee osteoarthritis: a multicenter, randomized, double-blind, sham-controlled trial. Osteoarthritis Cartilage. 2017;25(8):1247-1256.

Chapter 2 – System Overview

iovera° System Components

Handpiece (with storage cap)	Charging Dock
	
iovera° Smart Tip and Smart Tip Cap (STT2309 shown)	**Cartridge**
	

Electrical Adapter ("Charger")

WARNING!

Use only the electrical adapter (“charger”) and Charging Dock supplied with the iovera° system to charge the Handpiece.
To isolate the system from mains power, remove the adaptor from the mains socket.

Glossary

The terms and acronyms used in this guide are listed in the table below:

Term or Acronym	Description
Cartridge	A small, pressurized canister containing liquid nitrous oxide
Cartridge Holder	The space inside the Handpiece where the N_2O Cartridge is placed
Charging Dock	The stand used to hold the Handpiece during charging
Cooling Cycle	A single cryoanalgesia application using the iovera° system on a single site on a patient; One or more cooling cycles at different sites equal one treatment
Cryogen	A substance used to produce low temperatures; the iovera° system uses nitrous oxide (N_2O). Used interchangeably with refrigerant.
Handpiece	A non-sterile, reusable, handheld device designed to control the flow of refrigerant from a disposable Cartridge into an iovera° Smart Tip to cool target tissues
LCD Display	The color graphic information display at the back of the Handpiece
Main Button	Button located on the Handpiece that is used to start and to stop a cooling cycle; the button may also be used to perform other functions
Refrigerant	A substance used to produce low temperatures; the iovera° system uses nitrous oxide (N_2O). Used interchangeably with cryogen.
Reset Access	Located at the Handpiece Service Access Cover, this is an area that provides access to perform an iovera° system reset
RF Cannula Introducer	A needle introducer is a surgical device (rigid tube) used to provide a percutaneous (through the skin) tissue pathway to a targeted treatment site.
Skin Warmer	A plate located at the base of the needle(s) on the iovera° Smart Tip that is designed to keep the skin surface warm during a treatment; The STT2309 Smart Tip needles must be fully inserted for the skin warmer to be effective.
Smart Tip	The sterile tip that attaches to the end of the Handpiece to deliver a treatment. The iovera° Smart Tip Family is shown in Appendix G.
Smart Tip Cap, Guard	Protective cap that fully covers an iovera° Smart Tip when not in use
Storage Cap	Protective cap that can be used to cover the end of the Handpiece when a Smart Tip is not in use or when the Handpiece is charging
Treatment	One or more cooling cycles administered to one or more sites on a single patient

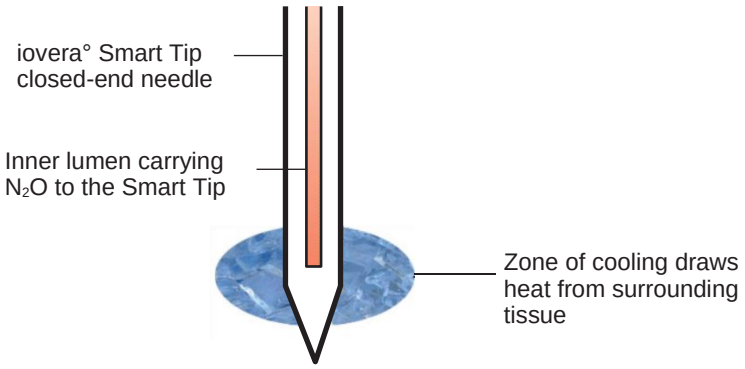
Theory of Operation

The Pacira Pharmaceuticals, Inc. iovera° system is a handheld device that uses closed-end needles (called Smart Tips) to treat the targeted peripheral nerves for a particular application. Cryoneurolysis has been well established as a successful and preferred non-toxic method of tissue destruction, while keeping the surrounding tissue structures intact. The iovera° consumables include nitrous oxide Cartridges and single-use iovera° Smart Tips.

During a patient treatment, the iovera° Smart Tip needle(s) are inserted into the target tissue and liquid nitrous oxide (N_2O) is delivered from a pressurized cylinder at >850 psi through a control valve and into the closed-end needles of the iovera° Smart Tip. Within each closed-end iovera° Smart Tip needle, the liquid nitrous oxide flows to the Smart Tip through an inner channel (lumen).

A combination of rapid pressure decreases, and evaporation of the nitrous oxide causes an endothermic event that rapidly draws heat from the surrounding tissue, thus causing focused cooling at the distal end of the inserted iovera° Smart Tip needle(s). The focused cooling can reach temperatures below -20 °C (-4 °F). By incorporating a skin warmer, the iovera° system focuses precise subdermal cooling while protecting the skin.

The iovera° Smart Tip closed-end needles leave nothing in the patient's body. The gas created from the evaporating N_2O is vented back up through the needle and released harmlessly into the atmosphere.



Sensors within the iovera° Handpiece monitor the automated delivery of nitrous oxide and the rate of cooling to ensure consistency during treatment cycles.

When applied to nervous tissue, this freezing power is known as cryoneurolysis; freezing along the nerve axon causes distal disintegration of the axon and breakdown of the myelin sheath, while keeping the endoneurium and other connective tissue elements intact, which helps the nerve to re-grow along its original pathway. Lesioning of the nerve axon at the point of contact with the iovera° Smart Tip needle end is caused by rapid freezing at or below -20°C (-4°F). The rapid freeze causes mechanical and osmotic stresses which disrupt the tissue within the freezing zone and create axonal discontinuity that results in an immediate cessation of nerve signaling. Subsequently, the distal segment of the axon and myelin sheath degenerate (through the process known as Wallerian Degeneration). The endoneurium, epineurium, and perineurium remain intact, allowing subsequent regeneration of the nerve. Cryoneurolysis has not been associated with secondary neuritis or neuroma formation in prior clinical Experience. [4]

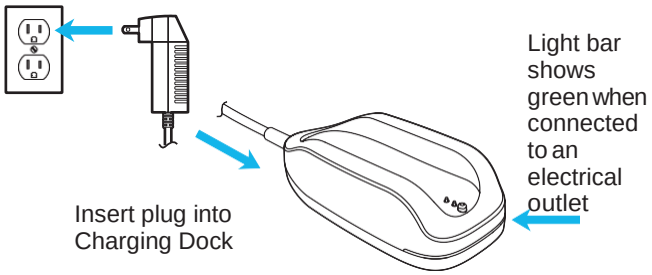
[4] Trescot, AM. Cryoanalgesia in an Interventional Pain Management Setting. *Pain Physician*. 2003;6:345-3

Chapter 3 – iovera° System Set-Up

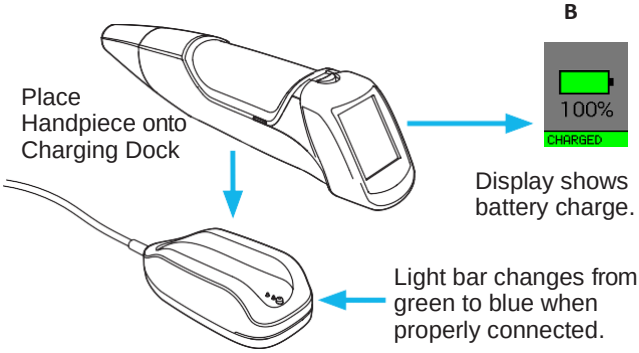
IMPORTANT	Although the battery of the iovera° system arrives partially charged, the amount of charge at delivery may vary. It is recommended that the Handpiece be **FULLY CHARGED** before first use.

Charging the Device

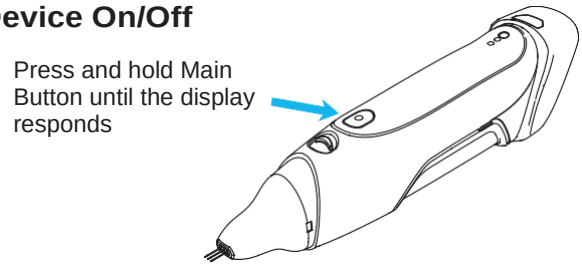
A. Plug adaptor into outlet
Plug charger cable into base of Charging Dock



B



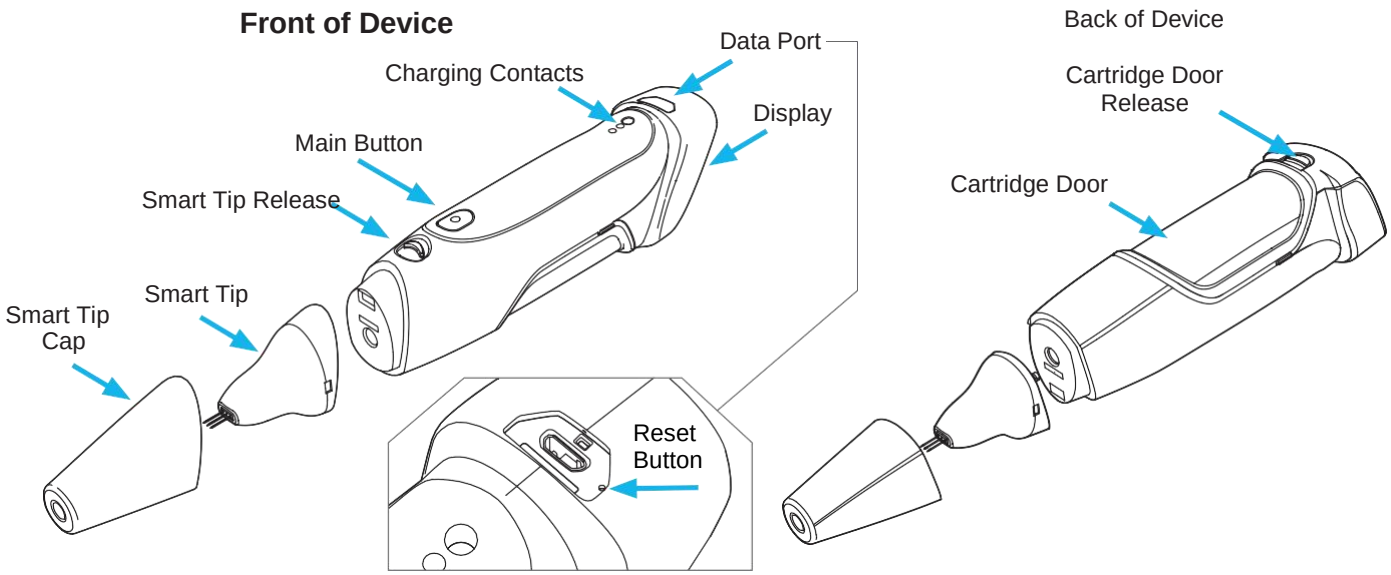
Turning the Device On/Off



iovera° Handpiece

The iovera° Handpiece is the control system that facilitates the transfer of nitrous oxide to the connected iovera° Smart Tip during treatment. The illustrations on the next two pages highlight the essential components of the Handpiece. To ensure that it is ready for use, always place the Handpiece into the Charging Dock when it is not in use.

Handpiece Components: Expanded View

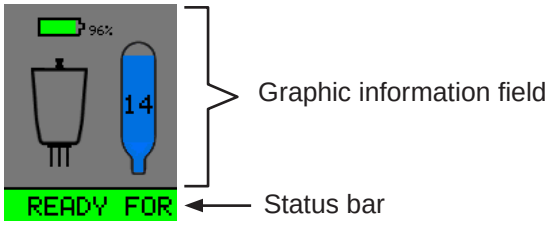


Information Display

The LCD display is an integral component of the iovera° system. The displays are context-sensitive and include 3 main types:

- Main display
- Treatment display
- Charging display

Each display type consists of two sections – a graphic information field and a status bar:



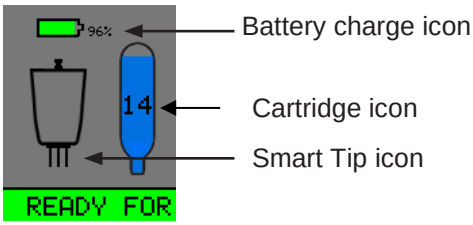
The messages on the status bar scroll to allow for sufficient content. The colors of the LCD status bar provide additional visual feedback of the Handpiece status:

- **Green** Normal operation
- **Yellow** Action indicated
- **Red** System issue requiring attention

Main Display

Cartridge icon:

- Number and height of **blue** field indicate how many cycles remain in the Cartridge for the current Smart Tip
- Icon flashes if a Cartridge is not detected.



Smart Tip icon:

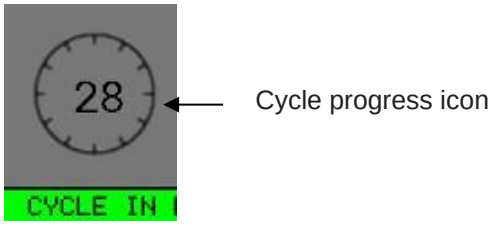
- Icon is solid when a Smart Tip is attached and functional
- Icon flashes when a Smart Tip is not attached

For battery charge icon, see **Battery Status** section below.

Treatment Display

Cycle progress icon:

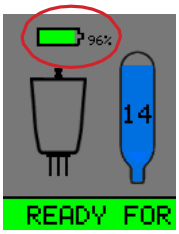
- Number indicates the number of seconds remaining in the current treatment cycle
- A check mark will appear if the cycle completes successfully.



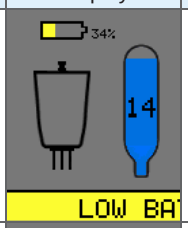
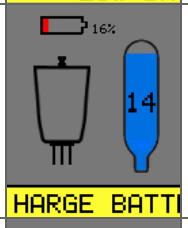
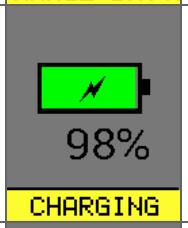
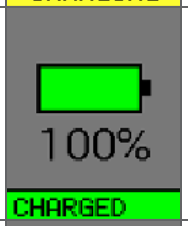
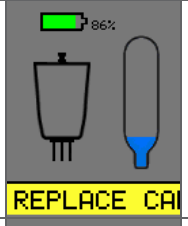
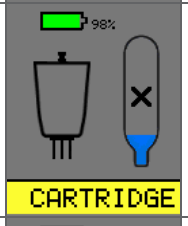
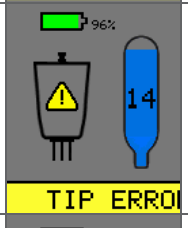
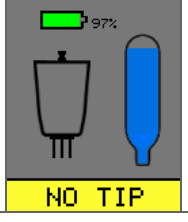
Battery Status

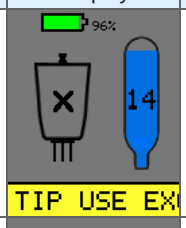
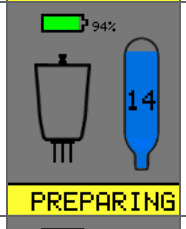
The LCD displays information indicating how much battery power is available as well as an indication that the battery is being charged.

During normal use, the system will display the battery charge level on the main display



Battery charge level is shown in **green** in the icon, as well as in text to the right of the battery

Message	Representative Display	Scrolling Text and Notes
LOW BATTERY		LOW BATTERY Note: The yellow battery bar also flashes. Message is displayed when battery charging is recommended.
RECHARGE BATTERY		RECHARGE BATTERY Note: Red battery bar also flashes Message is displayed when battery charge is insufficient to allow treatment cycles.
BATTERY CHARGING		CHARGING This display will appear when the Handpiece is receiving power from the Charging Dock. The Number shows current charge state of battery. The light bar on charger will appear blue during charging.
BATTERY CHARGED		CHARGED The light bar on charger will appear green at end of charging.
REPLACE CARTRIDGE		REPLACE CARTRIDGE The Cartridge icon shows minimum fill level without a cycle count. If the Cartridge is removed, an empty Cartridge icon flashes.
CARTRIDGE EXPIRED		CARTRIDGE EXPIRED Message is displayed if Cartridge has been left in the Handpiece too long.
TIP ERROR		TIP ERROR - *nn* Message is displayed if the tip is detected but is malfunctioning.
NO TIP		NO TIP The Tip icon flashes. The Cartridge icon will not display a cycle count (as count is tip-dependent) The blue cryogen level in icon will reflect current state.

Message	Representative Display	Scrolling Text and Notes
TIP USE EXCEEDED		TIP USE EXCEEDED Message is displayed if the smart tip has been used for its rated cycles.
PREPARING FOR CYCLE		PREPARING FOR CYCLE Message is displayed when system is warming the cryogen Cartridge prior to allowing a treatment cycle.
READY FOR CYCLE		READY FOR CYCLE The cryogen level and number in the Cartridge icon indicate the remaining cryogen and cycles in the Cartridge for the current Smart Tip The number flashes when 2 or fewer cycles remain.
CYCLE IN PROGRESS		CYCLE IN PROGRESS The number in the clock icon displays the seconds remaining in the current cooling cycle.
CYCLE COMPLETE		CYCLE COMPLETE This image is displayed for 2 seconds, then the display reverts to the main display (with Tip and Cartridge icons
CYCLE STOPPED (BY USER)		CYCLE STOPPED Message is displayed if user stops a cycle by pressing the Main Button while a cycle is in progress.
TILT HANDPIECE UP		TILT UP Message is displayed when angle of Handpiece is not vertical enough for treatment. Message is only displayed during treatment cycle.
SYSTEM FAULT		SYSTEM FAULT - *nn* Message is displayed when a critical failure with the system is detected such that treatment cycles are not allowed. “nn” is a two-digit error code.

Handpiece Control Features

Functions using the Main Button on the front of the iovera° Handpiece are described below:

Event	Action Description
Start a Cycle	Press and release the Main Button to initiate a cycle. **NOTICE** A cycle can only be initiated if the system detects an acceptable iovera Smart Tip, Cartridge, and sufficient battery charge
Stop a Cycle	Press and release the Main Button once after the cycle has started. Wait for the cycle to complete before withdrawing the needle(s) from the patient. **WARNING!** **Do not attempt to remove an inserted iovera° Smart Tip from a patient while treatment is in progress. Doing so could result in damage to subcutaneous tissue.**
Standby Mode	Press and hold the Main Button for several seconds to place the system in low-power standby mode. (The system will momentarily show a crescent moon display when entering standby mode.) **NOTICE** The iovera° Handpiece is shipped in standby mode. When the Handpiece remains unused for 40 minutes, it enters standby mode.
Wake Device from Standby Mode	When the Handpiece is in standby mode, press and hold the Main Button until the device wakes (display will show the "iovera°" start screen.) The system will wake from standby mode when placed into the Charging Dock.

Chapter 4 – Performing a Treatment Cycle

Setting up for a Treatment Cycle

Before initiating a treatment, ensure that the iovera° system is clean and disinfected. See the "Cleaning the iovera° System" section of this guide for details.

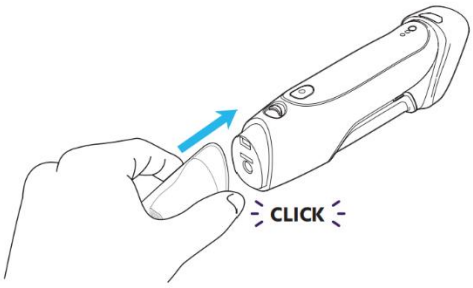
WARNING!	**Inspect all components prior to use. Do not use component if the component or its package appears damaged.**
WARNING!	**Physician discretion should be exercised when the patient presents with existing neuromuscular disease compromising the regeneration of peripheral nerves that may be involved in the treatment.**

Attaching the iovera° Smart Tip

WARNING!	**Carefully inspect the iovera° Smart Tip package prior to use for any breach of the sterile barrier or damage to the contents. If the sterile barrier integrity is compromised, or the contents are damaged, DO NOT USE, and contact a Pacira Pharmaceuticals, Inc. representative.**

1. Do not remove the Smart Tip Cap until preparation for Smart Tip insertion into the patient is complete.
2. Remove the iovera° Smart Tip from the sterile package and push it firmly into the Handpiece as shown (Figure A).
3. Gently tug on the inserted Smart Tip to ensure it is properly latched into the Handpiece.

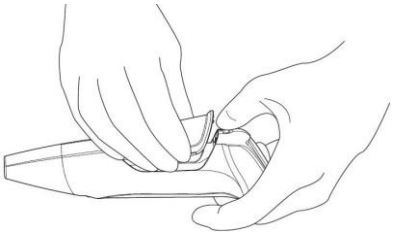
A. Align Smart Tip and connect onto Handpiece until clicked into place.



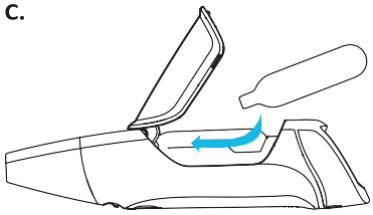
Inserting a Cartridge

1. Slide and hold the Cartridge door release towards the display end and open the cartridge door (Figure B).
2. Load Cartridge into the holder leading with the tapered end. The cartridge should sit level and click into place when properly inserted (Figure C).
3. Firmly close the door until the latch engages and clicks into place (Figure D).

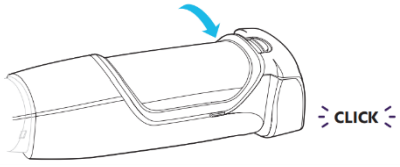
B.



C.



D.



NOTICE	To ensure optimum performance, a Cartridge will expire after being in the Handpiece for three hours. The Expired Cartridge symbol will appear on the display when the Cartridge expires.

NOTICE	Should a “Replace Cartridge” message be displayed shortly after a new cartridge has been installed, press and hold the main button to place the device in standby mode, then press and hold the main button again to wake the device.

NOTICE	To facilitate even heating of the cryogen after cartridge replacement, it is suggested that the Handpiece be held vertical, with the display facing up, and gently agitated until the “Ready or Cycle” message is displayed.

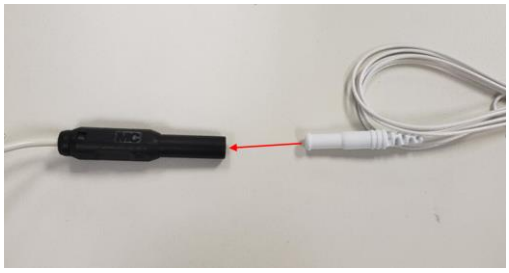
Nerve Targeting Using a Peripheral Nerve Stimulator

In applications where the target nerve is to be located without the aid of direct visualization, and/or where the use of anatomical landmarks requires additional confirmation, a separate off-the-shelf nerve stimulator device may be used to identify the target nerve with Smart tips that have the STIM designation.

WARNING!	**When using a nerve stimulator, follow the Instructions for Use (IFU) for that device, and observe all warnings, precautions, and contraindications.**

Connecting the Stimulation Compatible Smart Tip to a 3rd Party Nerve Stimulator

Fully insert insulated connector of the supplied Stimulating Tip Cable (P/N 12358) into the connecting cable receptacle of the 3rd party nerve stimulator as shown:



Fully insert the gold-plated end of the Stimulating Tip Cable into the receptacle in the Smart Tip housing as shown:

Inserting the iovera° Smart Tip into the Target Site

WARNING!	**The iovera° Smart Tip is sterile. Touching iovera° Smart Tip needles may compromise sterility. The Smart Tip comes protected in a Smart Tip Cap. DO NOT remove the Smart Tip Cap until ready to perform a cycle.**

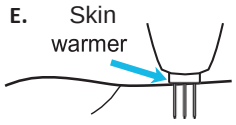
WARNING!	**Smart Tips are for single use only and cannot be re-sterilized.**

WARNING!	**Do not attempt to straighten or use kinked needles.**

1. Clean the treatment area with the antiseptic solution of choice.
2. Confirm the Handpiece is ready to start a cycle.
3. Remove the Smart Tip Cap: To remove the Smart Tip Cap, gently grasp the Smart Tip Cap from the ***top and bottom*** and pull away to remove.
4. Insert the iovera° Smart Tip into the target treatment site.

WARNING!	**Care should be taken when selecting the target treatment site. Treatment outside the intended target area could result in temporary loss of motor function or unintended freezing of surrounding structures.**

E.



5. In applications where skin warming at the base of the iovera° Smart Tip is necessary, such as for the STT2309 Smart Tip (refer to Smart Tip-specific instructions in Appendix C and D), ensure that the needles are fully inserted into the skin so that the skin warmer is contacting the skin (Figure E).

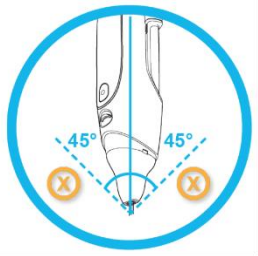
WARNING!	**Failure to insert the iovera° Smart Tip sufficiently may result in skin injury in percutaneous applications.**

6. If the Smart Tip has a minimum insertion depth mark on the needle, then the Smart Tip must be inserted into the tissue to at least the indicated minimum insertion depth to prevent skin damage (Figure F).

F.

Completing the Treatment Cycle

G.



1. Ensuring that the Handpiece is vertical or near vertical, Keep Handpiece upright (<45° away from perpendicular to the ground (Figure G), press and release the Main Button once to begin the cooling cycle. A tone sounds when the cycle begins.

WARNING!	**Minimize any movement of the Handpiece once the iovera° Smart Tip is in the desired position and the cooling cycle has started. Excessive movement could result in damage to subcutaneous tissue.**

WARNING!	**Do not attempt to remove the iovera° Smart Tip from the patient while cooling is in process. Doing so could result in damage to subcutaneous tissue.**

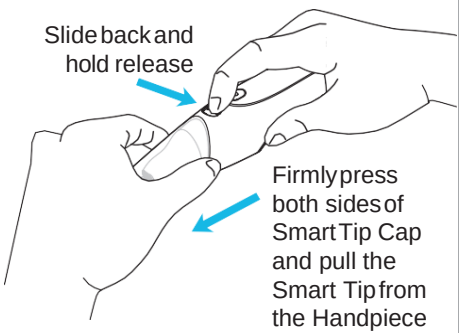
2. When the cycle starts, the LCD provides a countdown timer to indicate how many seconds remain in the cycle.
3. At the end of the cycle, the LCD will indicate that the cycle has completed, and a tone will sound. At this time, the iovera° Smart Tip may be removed from the treatment site and, if desired, repositioned at a different site for another treatment cycle.

WARNING!	**For percutaneous application, do not to treat the same site more than once within 10 minutes. For percutaneous applications, do not to treat the same site more than once within 10 minutes. This allows the skin to**

WARNING!	**Do not reposition or remove the iovera° Smart Tip if there is any resistance. This may indicate that the cooling zone is still attached to the iovera° Smart Tip and may result in damage to subcutaneous tissue if moved.**

4. When the treatment is complete, remove the iovera° Smart Tip from the patient.
5. Replace the Smart Tip Cap on the used Smart Tip.
6. Remove the Cartridge from the Handpiece.
7. While pressing the sides of the Smart Tip Cap, slide back and hold release button. Then, while pointing the Smart Tip in a safe direction, press both sides of the Smart Tip Cap and carefully remove the Smart Tip. (Figure H).
8. Place the used Smart Tip into a sharps container.
9. Clean the iovera° Handpiece (see section "Cleaning the iovera° System")
10. Clean the Charging Dock if necessary (see section "Cleaning the iovera° System").
11. Return the Handpiece to the Charging Dock.

H.



Stopping a Cycle

WARNING!	**Do not reposition or remove the iovera° Smart Tip from the patient if there is any resistance. This may indicate that the cooling zone is still attached to the iovera° Smart Tip and may result in damage to subcutaneous tissue if moved.**

If a cooling cycle must be terminated before the pre-programmed cycle is complete, press and release the Main Button on the Handpiece to terminate the cycle. Stopping a cycle may take a short time to complete to ensure safe removal of the iovera° Smart Tip.

WARNING!	**It is imperative that the user waits until the system signals that it is safe to remove the iovera° Smart Tip from the patient before doing so.** **a. The LCD indicates that the cycle has been canceled.** **b. A tone sounds as the cycle completes.**

Once the display indicates that the cycle has been canceled and the tone sounds, it is safe to remove the iovera° Smart Tip from the treatment area.

Performing an Emergency Cycle Stop

In the rare event that a cooling cycle fails to terminate, the Smart Tip may be released from the Handpiece while the cycle is in progress. Alternatively, the cryogen flow may be stopped by venting the Cartridge.

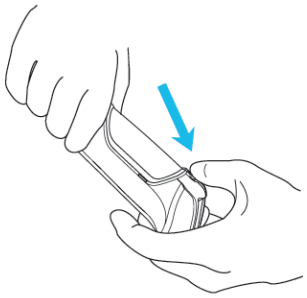
Be aware that a loud pop may be heard when the Smart Tip releases; this is expected.

⚠ WARNING!	**Do not reposition or remove the iovera° Smart Tip from the patient if there is any resistance. This may indicate that the cooling zone is still attached to the iovera° Smart Tip and may result in damage to subcutaneous tissue if moved.**

Removing the Cartridge

1. Replace Smart Tip Cap after completing treatment or prior to exchanging a Cartridge.
2. While wearing protective gloves, point the display end of the device away from the user, patient, and bystanders.

I.



3. Angle the Smart Tip up at 45 degrees and slide Cartridge door release towards display end (Figure I) Ensure the LCD end of the Handpiece is aimed in a safe direction.

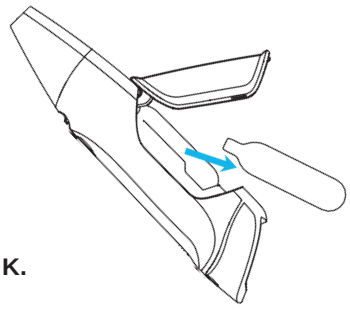
⚠ WARNING!	**If Smart Tip is removed before venting, venting may occur through the Handpiece outlet.**

4. Grip door near display and open at a slow controlled rate to vent N2O until hissing stops (Figure J). Keep hand away from door hinge while Cartridge is venting as exhausting N2O is very cold.
5. Open the door fully and remove the spent Cartridge (Figure K).

J.

⚠ **WARNING!**
Wear protective gloves while venting the Cartridge. Keep exposed skin away from door openings and door hinge while venting; the exhausting nitrous oxide can cause freeze burns.

K.



- If nitrous oxide continues to vent from the Cartridge, firmly hold the Cartridge and allow the nitrous oxide to vent completely (use gauze to insulate against cold if necessary).

WARNING!	**Nitrous oxide is under high pressure. A venting Cartridge may dislodge with high force if removed from the Handpiece before venting completes. Allow the system to depressurize completely before fully removing the Cartridge.**
CAUTION!	Exercise caution when removing the Cartridge.

6. Dispose of the used Cartridge following local requirements and protocols.

NOTICE	Always remove the Cartridge after completing treatment. If the Cartridge is left in the Handpiece for three hours, the Cartridge will expire. Replace the Cartridge prior to performing a treatment.

Cleaning the iovera System

The iovera° system (excluding the Smart Tip) is a reusable cryoneurolysis device and must be thoroughly cleaned and disinfected after each patient use. To clean the Handpiece:

- Remove contaminates with clean, pre-saturated 70% isopropyl alcohol (IPA) wipes. Repeat with new wipes until the device is clean.

NOTICE	It is important that the Handpiece be cleaned immediately after each patient use. Cleaning immediately after use helps prevent accumulation of contaminants.

⚠ CAUTION!	• Never submerge the iovera° Handpiece or the Charging Dock into any liquids. • Never use compressed air on, around, or in the iovera° Handpiece. • Do not allow liquids or particulates into the Cartridge chamber. Doing so could block nitrous oxide flow and prevent or limit cooling.

Detailed Instructions for Cleaning the Handpiece

Thoroughly cleaning the iovera° Handpiece involves the following:

- Remove conspicuous contamination. Inspect for any obvious signs of contamination (e.g., blood or other fluids, dirt/ debris, other obvious contaminants).
- Use clean, pre-saturated 70% IPA wipes. Vigorously scrub the contaminated areas until the contamination is removed. Repeat as required using a new clean wipe.
- Limit scrubbing to conspicuously contaminated areas to reduce the possibility of spreading contaminants around the device.
- Pay special attention to these areas on the Handpiece:
  - Small gaps and lines on the outer Handpiece shell.
  - Gaps around the Main Button, Smart Tip release actuator, and Cartridge door release actuator.
  - Areas around the Service Access Cover
- To ensure maximum disinfection, utilize sufficient fresh wipes to ensure that all surfaces remain damp per manufacturer's recommendations.
- Discard soiled wipe and obtain a new wipe as required.
- Once the visibly contaminated areas are clean, wipe the entire Handpiece gently.

When complete, return the Handpiece to the Charging Dock and allow it to air dry for at least 5 minutes prior to the next use.

Cleaning the Charging Dock

Use the same material and techniques described above to clean the Charging Dock.

Handpiece Storage

- If treatment is complete for the day, remove the Cartridge and discard it (see the Removing the Cartridge section).
- Return the Handpiece to the Charging Dock.

Chapter 5 – System Warnings and Troubleshooting

If the iovera° system detects an unfavorable condition, an error message with a red background will appear on the LCD display. Check the Troubleshooting section of this guide for additional information.

Troubleshooting

The following table contains instructions for basic troubleshooting actions. In the event device malfunctions persist or malfunctions occur beyond those described below, users should not attempt to repair the device. Contact Pacira Pharmaceuticals, Inc. Customer Service for guidance at the number shown below.

Issue	Possible Solution
Handpiece LCD is not on	• Press and hold the Main Button until the device wakes from standby mode. • If this does not resolve the issue, place the Handpiece on the Charging Dock, and check the battery status to ensure it has sufficient battery charge. • If the issue persists, perform a hard reset by inserting the end of a paper clip into the small hole for at least 2 seconds, and removing the paper clip, to reset the system (refer to Chapter 3, "iovera° System Setup" for the location of the reset button). If the issue persists, contact Pacira Technical Support at 855-793-9727.
Cycle will not start/ system indicates no Smart Tip is present	Remove and replace the Smart Tip. Confirm that the system detects that a Smart Tip is present. If the issue persists, contact Pacira Technical Support at 855-793-9727.
Cycle will not start/ system indicates Smart Tip error	Refer to the "iovera° Smart Tip Errors" section of the guide. NOTE: The device must be turned off and back on to clear the error.
Handpiece displays a System Fault error with a red background.	Refer to the "iovera° System Fault Errors" section of the guide.
System indicates a low battery condition with a yellow background	Battery power is low and a limited number of cooling cycles can be completed.
Handpiece will not charge or wakeup while in Charging Dock	Check the dock power to ensure the light bar on the dock is illuminated. Ensure the dock light changes color from green to blue when the Handpiece is placed on the dock. If not, make sure the Handpiece charging contacts are positioned correctly with the pins on the dock. Ensure the handpiece contacts and dock pins are free from debris and contamination. If the issue persists, perform a hard reset by inserting the end of a paper clip into the small hole for at least 2 seconds, and removing the paper clip, to reset the system (refer to Chapter 3, "iovera° System Setup" for the location of the reset button). If the issue persists, contact Pacira Technical Support at 855-793-9727.
Handpiece is leaking cryogen (may hear hissing)	Contact Pacira Technical Support at 855-793-9727 with details.
System indicates treatment was canceled	The treatment cycle was canceled (button was pressed or an error was detected). Wait until the system indicates the cycle is complete before attempting to remove the Smart Tip from the patient.

iovera° System Fault Errors

NOTICE	All messages appear as scrolling text on the LCD screen.

System Fault Error Number	Meaning	What To Do
11 or 13	Valve failed to open during treatment	Turn the device off and on to clear the error. If the error occurred following Cartridge venting, **wait at least 5 minutes** before attempting the next cooling cycle.
14	Valve leak detected after previous valve closure confirmed	Turn the device off and on to clear the error.
15	Cartridge temperature exceeded 38°C	Turn the device off and on to clear the error. If the problem persists, turn off the device, replace the Cartridge, then turn the device back on.
16	Difference between Cartridge heater temperatures too great	Turn the device off and on to clear the error.
17	Cartridge pressure exceeded 1200 psi	Turn the device off and on to clear the error. If the problem persists, turn off the device, replace the Cartridge, then turn the device back on.
18	Flash memory initialization failure	Contact Pacira Technical Support at 855-793-9727.
19	Persistent data in incorrect format	
20	Persistent data version too old	
21	Calibration data corrupted	
22	Reboot times exceeded	Turn the device off and on to clear the error.
23	Cartridge temperature(s) exceeded hard limit	Turn the device off, wait at least ten minutes, then turn the device back on to clear the error.
24	Valve failed to close during treatment	**Vent the Cartridge or remove the Smart Tip from the Handpiece immediately**. Contact Pacira Technical Support at 855-793- 9727.
25	Cartridge took too long to reach correct temperature	Turn the device off and on to clear the error. If the problem persists, replace the Cartridge.
26	Cartridge thermistor 1 fault	Contact Pacira Technical Support at 855-793-9727.
27	Cartridge thermistor 2 fault	
28	Upstream pressure fault	
29	Downstream pressure fault	

Pacira Pharmaceuticals, Inc. recommends that users fully charge the system prior to first use. Training on the operation and specific techniques is provided by Pacira Pharmaceuticals, Inc., and/or your local representative.
See contact information on the back cover of the user guide.

There are no user-serviceable parts in the iovera° system. Contact Pacira Customer Support.

If any of the above System Fault errors persist, contact Pacira Technical Support at 855-793-9727

iovera° Smart Tip Errors

NOTICE	All messages appear as scrolling text on the LCD screen.

Smart Tip Error Number	Meaning	What To Do
11	Smart Tip temperature out of range	Turn the device off and on or detach and re-attach the Smart Tip to clear the error. Ensure the Smart Tip is correctly inserted into the patient during treatment. If the problem persists, replace the Smart Tip.
12	Smart Tip preheat timeout during cycle (Smart Tip did not reach temperature in allotted time)	Turn the device off and on or detach and re-attach the Smart Tip to clear the error. If the problem persists, replace the Smart Tip.
13	Smart Tip failed initial test upon insertion	
14	Smart Tip temperature(s) exceeded operating limits	Turn the device off and on or detach and re-attach the Smart Tip to clear the error. Wait at least 10 minutes to allow the Smart Tip temperature to recover. If the problem persists, replace the Smart Tip.
15	Smart Tip temperature(s) exceeded hard limit	
16	Smart Tip authentication challenge message failed CRC check	Turn the device off and on or detach and re-attach the Smart Tip to clear the error. If the problem persists, replace the Smart Tip.
17	Smart Tip failed authentication	
18	Smart Tip descriptor message failed CRC check	
19	Smart Tip/Handpiece incompatibility detected	
20	Smart Tip descriptor version mismatch	
22	Smart Tip secure processor reset count exceeded	
23	Smart Tip occlusion	Turn the device off and on to clear the error. Detach and re-attach the Smart Tip to relieve any trapped pressure. If the problem persists, replace the Smart Tip.
24	Smart Tip thermistor 1 fault	Turn the device off and on or detach and re-attach the Smart Tip to clear the error. If the problem persists, replace the Smart Tip.
25	Smart Tip thermistor 2 fault	
26	I^2C timeout error	
27	I^2C reset error	
28	Difference between Smart Tip temperature sensors too great	Turn the device off and on or detach and re-attach the Smart Tip to clear the error. Ensure the Smart Tip is correctly inserted into the patient during treatment. If the problem persists, replace the Smart Tip.

If any of the above Smart Tip errors persist, contact Pacira Technical Support at 855-793-9727.

Chapter 6 – Appendices

Appendix A – Guidance and Manufacturer's Declaration

Table 1 Guidance and Manufacturer's Declaration – Electromagnetic Emissions		
The iovera° system is intended for use in the electromagnetic environment specified below. The customer or the user of the iovera° system should ensure that it is used in such an environment.		
Emissions Test	**Compliance**	**Comments**
Conducted Emissions CISPR 11:2015+A1:2016+A2:2019	Class B 150 kHz to 30 MHz	The iovera° system uses RF energy only for its internal function. Therefore, its RF emissions are very low and are not likely to cause any interference in nearby electronic equipment.
Radiated Emissions CISPR 11:2015+A1:2016+A2:2019	Class B 30 MHz to 1 GHz	
Harmonics IEC 61000-3-2:2019+A1:2021	Per Clause 5 of the standard	
Flicker IEC 61000-3-3:2013+A2:2021	Per Clause 5 of the standard	

Table 2 Guidance and Manufacturer's Declaration – Electromagnetic Immunity			
The iovera° system is intended for use in the electromagnetic environment specified below. The customer or the user of the iovera° system should ensure that it is used in such an environment			
Test Type	**IEC 60601 test level**	**Compliance Level**	**Electromagnetic Environment – Guidance**
Electrostatic discharge (ESD) IEC 61000-4-2	±8 kV contact discharge ±2, 4, 8 & 15 kV air discharge	±8 kV contact discharge ±2, 4, 8 & 15 kV air discharge	Floors should be wood, concrete, or ceramic tile. If floors are covered with synthetic material, the relative humidity should be at least 30%.
Radiated Immunity IEC 61000-4-3	80 MHz - 2.7 GHz 3 V/m, 80% modulation @ 1 kHz	80 MHz - 2.7 GHz 3 V/m, 80% modulation @ 1 kHz	Portable RF communications equipment (including peripherals such as antenna cables and external antennas) should be used no closer than 30 cm (12 inches) to any part of the iovera° system, including cables specified by the manufacturer. Otherwise, degradation of the performance of this equipment could result.
Proximity field from RF wireless communications equipment IEC 61000-4-3	Spot frequencies, 385 MHz – 5.750 GHz, Pulse Modulation	Spot frequencies, 385 MHz – 5.750 GHz, Pulse Modulation	
Conducted Immunity (AC Power) IEC/EN 61000-4-6	0.15 - 80 MHz: 3 Vrms ISM bands: 6 Vrms 80% AM modulation @1 kHz on AC Mains	0.15 - 80 MHz: 3 Vrms ISM bands: 6 Vrms 80% AM modulation @1 kHz on AC Mains	Mains power quality should be that of a typical commercial or hospital environment.
Electrical Fast Transients (AC Power) IEC 61000-4-4	±2 kV (AC Mains) 5/50 ns pulses@100 kHz (15 ms bursts repeated every 300 ms)	±2 kV (AC Mains) 5/50 ns pulses@100 kHz (15 ms bursts repeated every 300 ms)	Mains power quality should be that of a typical commercial or hospital environment.
Surge Line to Line (AC Power) IEC 61000-4-5	±1 kV Line to Line ±2 kV Line to Ground	±1 kV Line to Line ±2 kV Line to Ground	Mains power quality should be that of a typical commercial or hospital environment.
Magnetic Immunity IEC 61000-4-8	3 A/m 50/60 Hz	3 A/m 50/60 Hz	Power frequency magnetic fields should be at levels characteristic of a typical location in a typical commercial or hospital environment.
Voltage Dips and Interruptions IEC 61000-4-11	0% UT 0.5 cycle 0% UT 1 cycle 0% UT 5 sec 70% UT 25 cycles	0% UT 0.5 cycle 0% UT 1 cycle 0% UT 5 sec 70% UT 25 cycles	If the user of the iovera° system requires continued battery charging operation during power mains interruptions, it is recommended that the Charging Dock be powered from an uninterruptible power supply.

NOTE: UT is the AC mains voltage prior to application of the test level

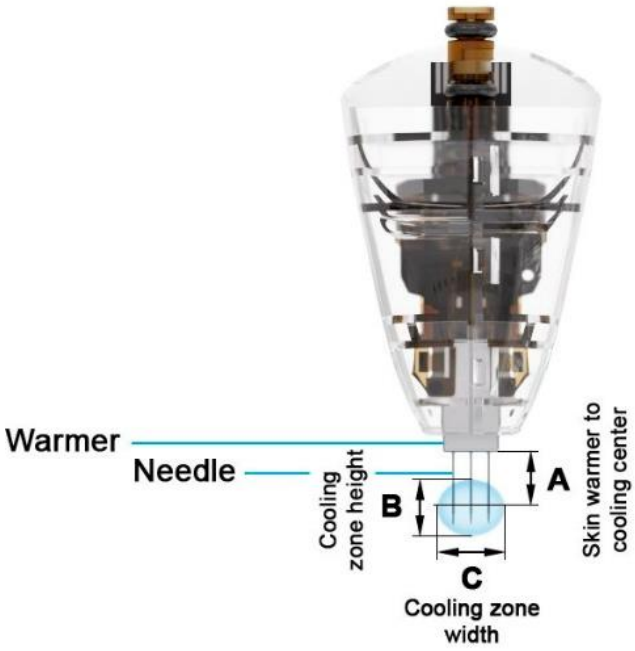
Appendix B – System Specifications

Model	HPT2221
Handpiece Mass	252 g (0.555 lbs.)
Charging Dock Mass	205 g (0.452 lbs.)
Intrusion Protection Rating	IPX0 – no protection against fluid ingress
Type of Refrigerant Used	Nitrous Oxide (N2O)
Minimum/Maximum Internal Operating Pressure	5650 to 6880 kPa (820 to 998 psi)
Power Requirements	Input: 100 - 240 VAC, 50/60 Hz, 0.35 – 0.15 A Output (power adapter): 5 VDC, 2.5 A Power adapter: XP Power ACM18US05 or equivalent
Internal Battery (not serviceable)	3.7V 3100mAh
Duty Cycle	Capable of continuous operation between charging cycles
Replaceable Parts	Piercing point/Filter assembly
Refrigerant Containers	Only use Pacira Pharmaceuticals, Inc. provided refrigerant Cartridges (iovera° Cartridges)
Electrical Mains Adapters	Only use Pacira Pharmaceuticals, Inc. provided electrical mains adapter for the Charging Dock
Thermal Insulation	Handpiece is designed to prevent excessive cooling, heating, and possible injury to the user
Applied Temperatures	Minimum: -88°C (Needle cooling center, absolute minimum) Maximum: 52°C (Skin warmer, single fault condition)
Acoustic Levels	Maximum: 83 dBA
Electrical Isolation	Type  BF Applied Part· Note: To isolate the iovera° system from mains power, unplug the power adapter from the wall outlet

Operating, Storage, and Transit Conditions:

	Operating	Storage and Transit
Temperature	15 - 28°C (59 ~ 82°F)	-20 - 50°C (-4 ~ 122°F)
Humidity	30 ~ 60% RH	10 ~ 85% RH
Pressure	76 ~ 102kPa (11 ~ 14.8psi)	50 ~ 106kPa (7 ~ 15.4psi)

Appendix C – Smart Tip (3x8.5 mm Sharp, 27 Gauge)



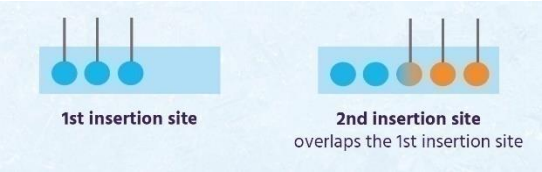
	A mm (in)	B mm (in)	C mm (in)
STT2309	6.3 mm (0.25 in)	6.6 mm (0.26 in)	7.9 mm (0.31 in)

Dimensions are for information purposes only. They are based on a 33-second cooling cycle performed in agarose gel. The ice ball size could vary based on anatomy/physiology of patients and should not affect the efficacy of treatment.

Procedure

Insert the Smart Tip needles until the skin warmer is in contact with the skin, then perform a cooling cycle.

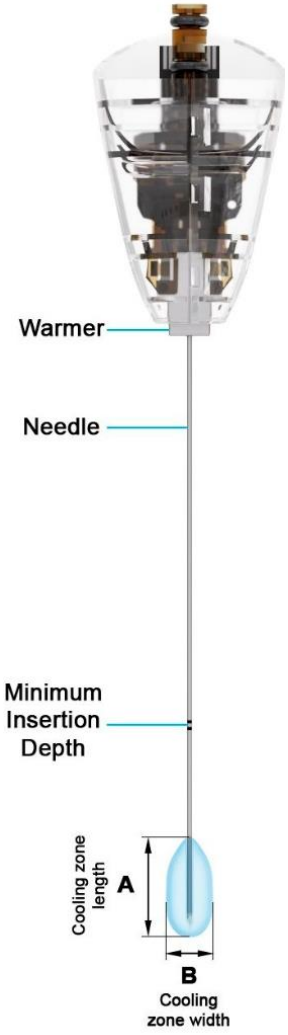
Overlap next cycles by one insertion site:



Note: The skin warmer heats the skin immediately adjacent to the cooling area. The smart tip needle cools the surrounding tissue as described by the ice ball dimensions.

WARNING! To reduce the likelihood of skin injury, the skin warmer must be pressed against the skin when the needle is inserted before running a cooling cycle.

Appendix D – Smart Tip (1x90 mm Sharp, 20 Gauge)



	mm (in)	
	A	B
STT2190	15.5 mm (0.61 in)	7.5 mm (0.30 in)

Dimensions are based on a 60-second cooling cycle performed in agarose gel. The ice ball size could vary based on anatomy/physiology of patients and should not affect the efficacy of treatment.

WARNING! To reduce the likelihood of skin injury, insert the needle at least 30 mm, denoted by the double marking (labeled minimum insertion depth on the image).

WARNING! During the iovera cooling cycle, a cooling zone is formed on the outer surface of the needle. The cooling cycle progress is displayed on the LCD screen of the iovera° Handpiece. Once the cooling cycle is complete, the iovera° Smart Tip needle should remain in place until no resistance is felt upon removal.

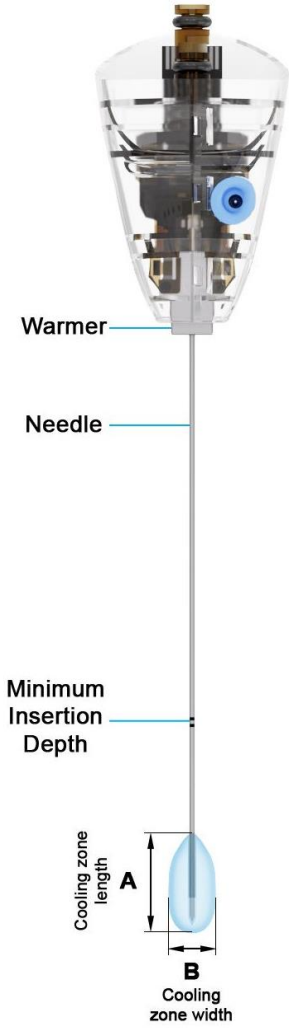
CAUTION! Small bend radii may affect performance.

- Do not kink or permanently deform the needle.
- The minimum bend radius is 55 mm.

Procedure

- Pre-piercing of the skin may ease Smart Tip insertion.
- Insert the needle into the desired location, ensuring it passed the minimum insertion depth, and then initiate the cooling cycle.

Appendix E – Smart Tip (1x90 mm Sharp, 20 Gauge) with Nerve Stim



	mm (in)	
	A	B
STT2190STIM	15.5 mm (0.61 in)	7.5 mm (0.30 in)

Dimensions are based on a 60-second cooling cycle performed in agarose gel. The ice ball size could vary based on anatomy/physiology of patients and should not affect the efficacy of treatment.

WARNING! To reduce the likelihood of skin injury, insert the needle at least 30 mm, denoted by the double marking (labeled minimum insertion depth on the image).

WARNING! During the iovera cooling cycle, a cooling zone is formed on the outer surface of the needle. The cooling cycle progress is displayed on the LCD screen of the iovera° Handpiece. Once the cooling cycle is complete, the iovera° Smart Tip needle should remain in place until resistance is not felt upon attempting removal.

CAUTION! Small bend radii may affect performance.

- Do not kink or permanently deform the needle.
- The minimum bend radius is 55 mm.

Procedure

- Pre-piercing of the skin may make Smart Tip insertion easier.
- Insert the needle into the desired location, ensuring it passed the minimum insertion depth, and then initiate the cooling cycle.

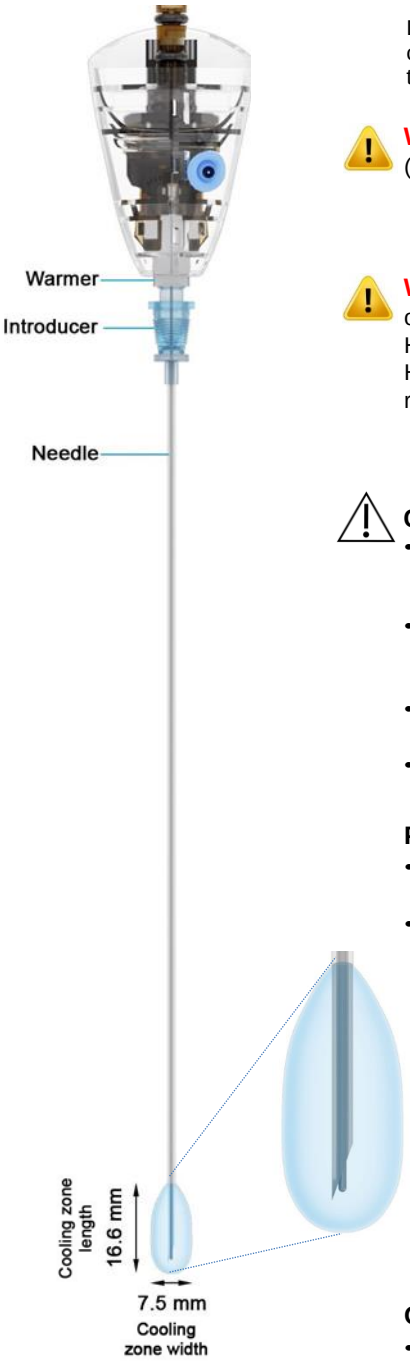
Optional Nerve Stimulation

- This iovera° Smart Tip is equipped to be connected to a separate off-the-shelf compatible nerve stimulator via the port on the side of the Smart Tip using the cable provided.
- Please refer to manufacturer-specific instructions for that device and observe all warnings, cautions, and precautions should the user choose to use this optional feature.

Appendix F – Smart Tip (1x180 mm Blunt, 25 Gauge) with Nerve Stim

	mm (in)	
	A	B
STT21180STIM	16.6 mm (0.65 in)	7.5 mm (0.29 in)

Dimensions are based on a 70-second cooling cycle performed in agarose gel. The ice ball size could vary based on anatomy / physiology of patients and should not affect the efficacy of treatment.



WARNING! The Smart Tip is designed to work with 3rd party manufactured radiofrequency (RF) 20-gauge sharp introducers, 15 cm in length, with 10mm straight or curved tips.

WARNING! During the iovera cooling cycle, a cooling zone is formed on the outer surface of the introducer. The cooling cycle progress is displayed on the LCD screen of the iovera° Handpiece. Once the cooling cycle is complete, the iovera° Smart Tip can be removed. However, the introducer should remain in place until resistance is not felt upon attempting removal.

CAUTION!

- The STT21180STIM Smart Tip needle is flexible, and deformation is acceptable if the needle can pass through the introducer and the needle lumen is not compromised (kinked/crimped).
- Using a 20 Gauge introducer shorter than 15 cm is not recommended. Shorter introducers may not provide sufficient support for the needle, potentially resulting in permanent kinking or crimping.
- Injury to soft tissue or the nerve can be caused by withdrawing the Introducer prior to sufficient thawing of the cooling zone.
- Please refer to 3rd party manufacturer-specific instructions for the introducer and observe all warnings, cautions, and precautions.

Procedure

- A Radiofrequency (RF) introducer provides a path for the Smart Tip to the target nervous tissue.
- Before Introducer placement, it is recommended to insert the Smart Tip into the introducer until it is flush with the tip of introducer. This ensures proper fit and determines the necessary insertion depth to prevent the needle from protruding beyond the introducer.

  Target nervous tissue using a 3rd party Introducer; confirm introducer placement through fluoroscopic, ultrasound, or any standard of care imaging technology or Nerve Stimulator.

  Gently insert the Smart Tip needle until flush with the pre-placed introducer's tip.

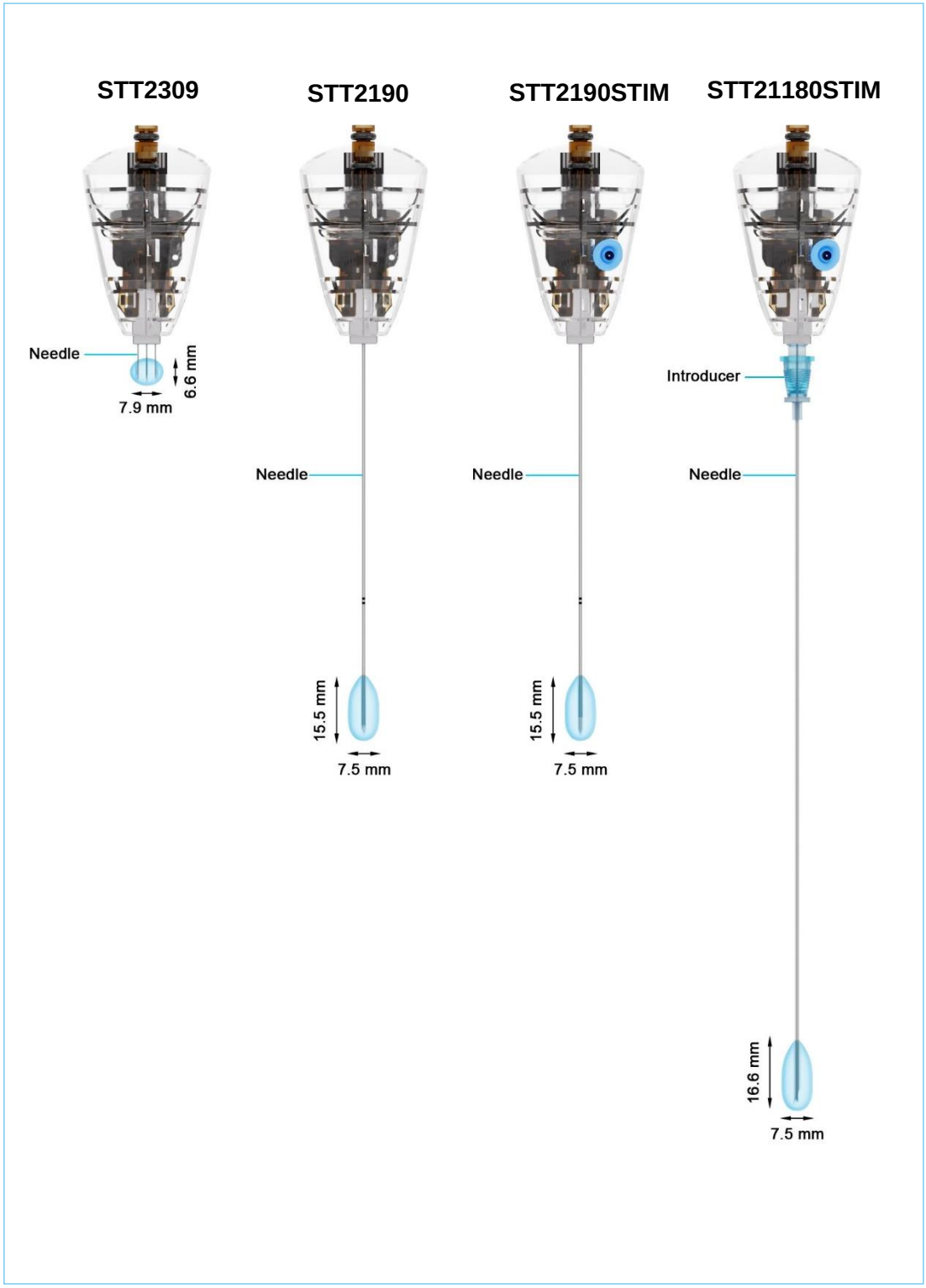
  Initiate a cooling cycle, ensuring the Handpiece remains stable throughout the treatment. It is recommended to hold the iovera° Handpiece in one hand while steadying the introducer with the other.

  When the treatment cycle is completed, as indicated on the Handpiece Display, securely stabilize the RF introducer, and remove the Smart Tip from the introducer. The iovera° Smart Tip can be removed upon completion of the cooling cycle. The introducer should be left in place until no resistance is felt upon its removal.

Optional Nerve Stimulation

- The iovera° Smart Tip must be used with an insulated RF introducer for Nerve Stimulation.
- The iovera° Smart Tip connects to a separate compatible 3rd party nerve stimulator via the port on the side of the Smart Tip using the stimulation cable provided.
- Please refer to manufacturer-specific instructions for the nerve stimulator and observe all warnings, cautions, and precautions should the user choose to use this optional feature.

Appendix G – iovera° Smart Tip Family



Appendix H – Cybersecurity Considerations

The iovera° System has the following Cybersecurity considerations:

- The System does not require user authentication for operation. It is ready for use as soon as required operation parameters are met.
- The System does not incorporate wireless communications.
- The SD card port is inactive.
- The USB port is for Pacira use only; it presents as a read-only Mass Storage Device when connected to a computer and is used for log retrieval.
- The Smart Tip interface is proprietary and encrypted.
- The System does not require IT connectivity at the clinical setting.
- The System software is not field upgradeable – devices must be returned to Pacira for upgrade. Customers will be notified in the event of upgrades due to cybersecurity findings.
- Since there are no user-manageable assets, a Software Bill of Materials is not provided.
- The System does not contain Protected Health Information or Personally Identifiable information.
- The System does not contain any form of Operating System and is therefore not subject to commonly exploited vulnerabilities in commercially available Operating Systems.
- Devices that have reached the end of their usable lifetimes should be returned to Pacira for disposal and removal of Pacira proprietary information.

PACIRA

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