NanoKnife 3.0

Irreversible Electroporation (IRE)

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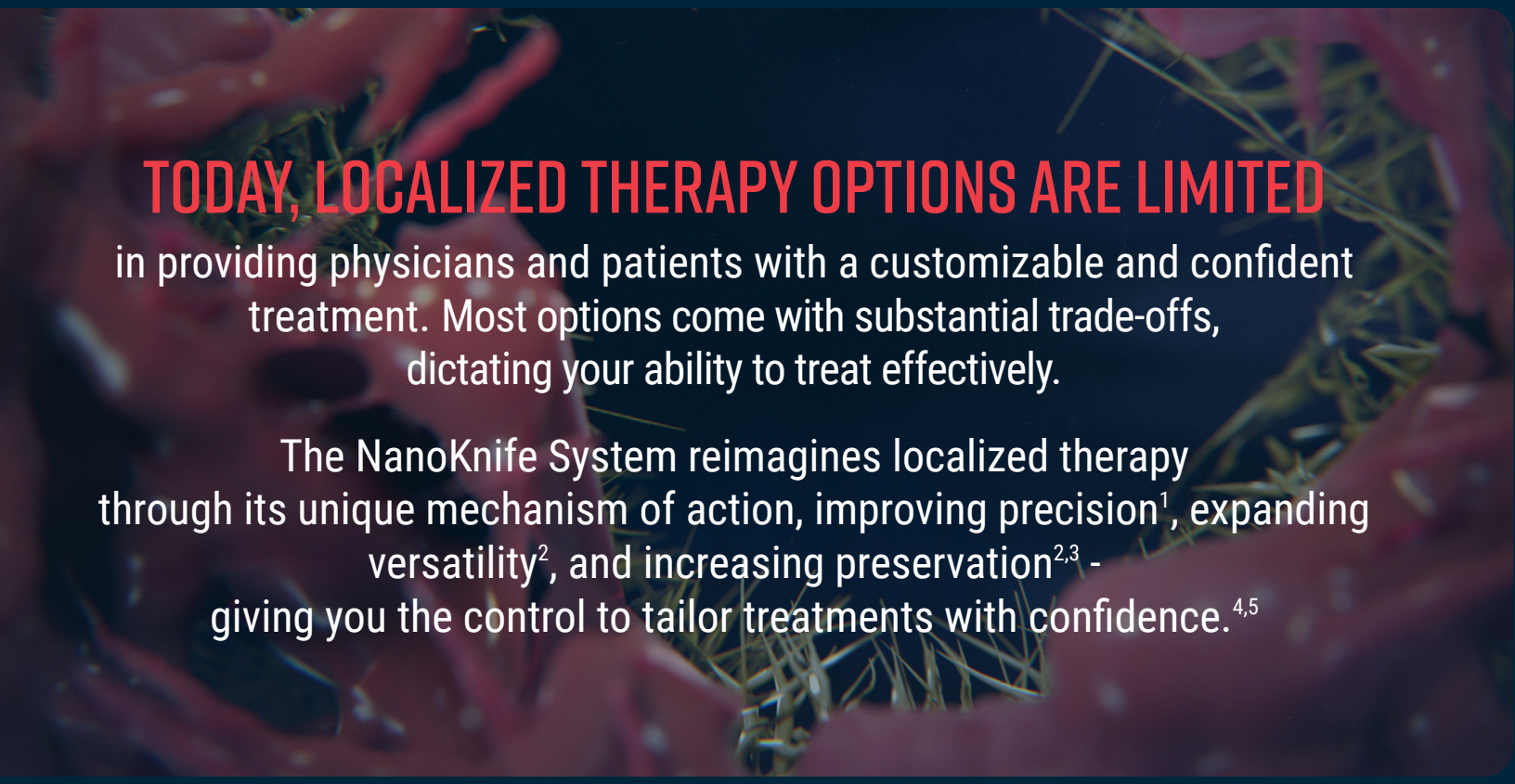

TODAY, LOCALIZED THERAPY OPTIONS ARE LIMITED

in providing physicians and patients with a customizable and confident treatment. Most options come with substantial trade-offs, dictating your ability to treat effectively.

The NanoKnife System reimagines localized therapy through its unique mechanism of action, improving precision[1], expanding versatility[2], and increasing preservation[2,3] - giving you the control to tailor treatments with confidence.[4,5]

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Harnesses the power of Irreversible Electroporation (IRE) to effectively destroy targeted cells without the use of thermal energy.[6]

Delivers high-voltage pulses to create permanent nanopores within the cell membrane. This stimulus induces an apoptotic-like cellular death in the targeted tissue, resulting in a complete ablation.[7,8]

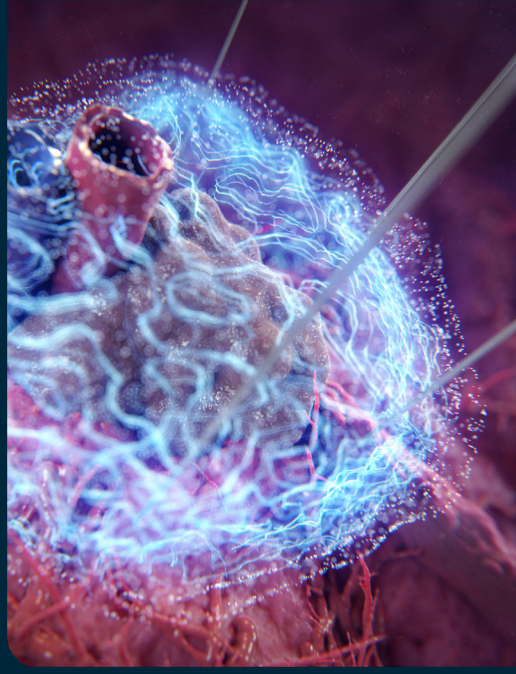
Electrodes can be deployed in multiple configurations providing precise and customizable ablation zones.[1]

Sharp demarcation of IRE-ablated zone is well-visualized immediately during the procedure using real-time ultrasound imaging.[9]

PRECISION EMPOWERED.

The NanoKnife System gives you, the physician, the ability to sculpt and control the ablation zone through a variety of electrode configurations.[1]

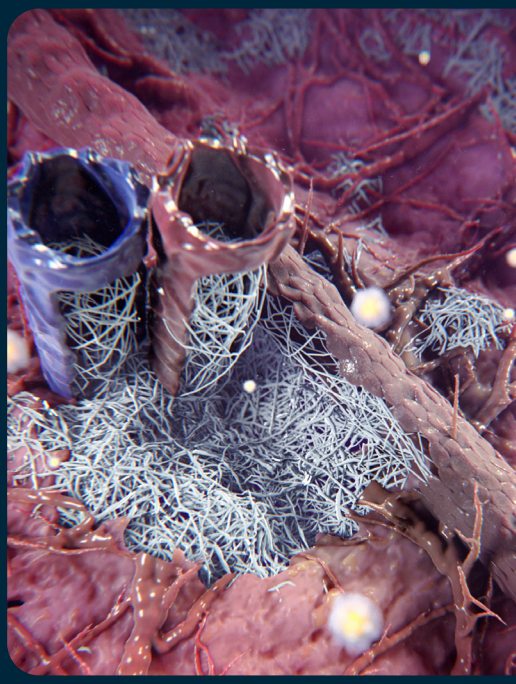
IRE effectively destroys the targeted tissue and gives you precise treatment margins resulting in confident treatment coverage for your procedure.[4,5]



PRESERVATION REDEFINED.

The procedure spares vital structures by retaining the structural integrity of the targeted tissue.[2,3]

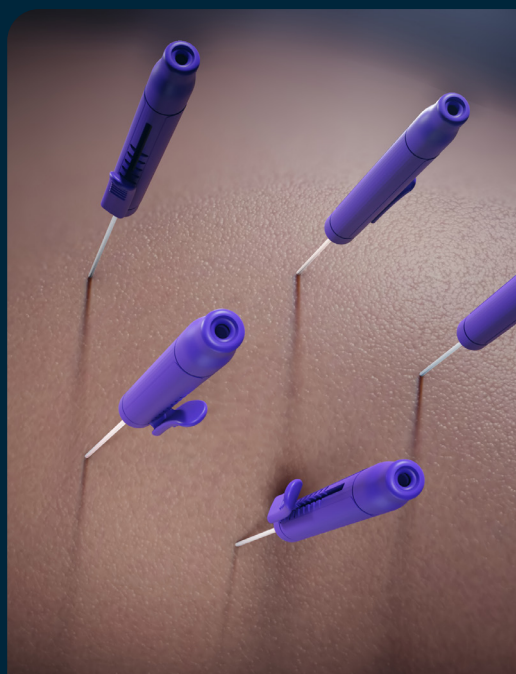
The delivery of non-thermal energy allows for the preservation of the extra-cellular matrix, facilitating post-ablation, histological and functional tissue regeneration.[2,3]



VERSATILITY PERFECTED.

Multiple electrode configurations, coupled with a unique mechanism of action, allow the device to be used in all segments of an organ to optimize treatment delivery.[2]

Electrodes can be confidently placed near vital structures, maximizing your ability to personalize treatment to your patient's anatomy. [4,5]



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YOUR TREATMENT REIMAGINED.

THE NANOKNIFE 3.0 SYSTEM

US Part Numbers	International Part Numbers	Description
H78720300301US0	H787203003010	NanoKnife 3.0 Generator
H787204001090	H787204001030	NanoKnife Single Electrode Activation Probe 15 cm
H787204001100	H787204001050	NanoKnife Single Electrode Activation Probe 25 cm
H787204003015	H787204003015	NanoKnife Single Electrode Probe Spacer (Pack of 10)

References

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6. Maor E. et al., The effect of irreversible electroporation on blood vessels, Technol. Cancer Res. Treat.6(4), 307–312 (2007).10.1177/153303460700600407.

7. Bower M, Sherwood L, Li Y, Martin R. Irreversible electroporation of the pancreas: definitive local therapy without systemic effects. J Surg Oncol. 2011 Jul 1;104(1):22-8. doi: 10.1002/jso.21899. Epub 2011 Feb 28. PMID: 21360714.

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9. Lee EW, Chen C, Prieto VE, Dry SM, Loh CT, Kee ST., Advanced hepatic ablation technique for creating complete cell death: irreversible electroporation. Radiology 255:426–433. (2010). doi: 10.1148/radiol.10090337.

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Important Risk Information

Indication For Use
US: The NanoKnife System with six outputs is indicated for surgical ablation of soft tissue.

Canada: The NanoKnife System is a medical device for cell membrane electroporation. Electroporation is a phenomenon that occurs in cell membranes as cells are exposed to an electrical field of sufficiently high intensity. The electric field acts as a physical stimulus, bringing about alterations in cell membranes that result in increased permeability.

EU: The NanoKnife System is indicated for the ablation of prostate tissue in patients with intermediate risk prostate cancer.

Contraindications:
- Ablation procedures using the NanoKnife System are contraindicated in the following cases:
- Ablation of lesions in the thoracic area in the presence of implanted cardiac pacemakers or defibrillators
- Ablation of lesions in the vicinity of implanted electronic devices or implanted devices with metal parts.
- Ablation of lesions of the eyes, including the eyelids.
- Patient history of Epilepsy or Cardiac Arrhythmia
- Recent history of Myocardial Infarction.

Warnings:
- **EU Only:** The NanoKnife device has been evaluated for the ablation of prostate tissue in patients with intermediate risk prostate cancer. The use of this device in other organs for other disease states has not been fully evaluated.
- Clinical Issues (including Arrhythmia, Hypertension, and Thrombus Risks)
- Patients with Q-T intervals greater than 500 ms (milliseconds) are at an increased risk for inappropriate energy delivery and arrhythmia. Verification of proper function of a synchronization device before initiating energy delivery is essential in these patients.
- Asynchronous energy delivery (90 PPM (Pulses Per Minute)) might trigger atrial or ventricular fibrillation, especially in patients with structural heart disease. Ensure that proper interventions (e.g. defibrillator) and appropriately trained personnel are readily available for dealing with potential cardiac arrhythmias.
- Using QRS synchronization devices whose output is not compatible with the specifications listed in this manual may result in arrhythmias including ventricular fibrillation.
- Adequate precautions should be taken for patients with implantable electrical devices. Note the contraindication in certain patients.
- There are potential risks associated with the location of the ablation: near the pericardium (tachycardia), or near the vagus nerve (bradycardia).
- Additional patients may be at risk with insufficient muscle blockade or anesthetic analgesia (reflex tachycardia and reflex hypertension); patients with abnormal sinus rhythm prior to an ablation (arrhythmia); patients with a history of hypertension (hypertension); or patients with partial portal venous thrombosis, low central venous pressure (CVP), and a prothrombotic condition (venous thrombosis).

Use of Electrodes:
- Avoid repeated vascular insult during electrode placement.
- As anticipated with a needle-related procedure, repeated vascular insult due to multiple insertions into a vessel by an electrode during electrode placement may cause thrombus.
- Ensure continuous image guidance during the needle placements. Failure to do so can lead to traumatic injury to surrounding structures.
- Care should be taken during electrode placement in areas that require tissue be separated or retracted to avoid surrounding tissue damage.
- To avoid risks of infection, always maintain the electrodes' protective packaging (cap, tubes, etc.) when the electrodes are not placed in the patient.
- Only electrode probes with intact electrical insulation must be used. Any electrodes with damaged electrical insulation must be discarded immediately and not connected to the NanoKnife Generator.
- To preserve the electrode's sterility do not remove the electrodes from the packaging until the User is ready to apply the electrode to the patient.
- Do not use the electrodes after the expiration date printed on their packaging. Observe the electrodes manufacturer's specific instructions (e.g., printed on the electrodes' packaging).
- Only use AngioDynamics Electrode Probes with the NanoKnife System Generator.
- Maintain electrical separation of the electrodes from safety ground by doing the following
- Disconnect any electrode from the Generator that is not applied to the patient.
- Avoid any clamping of the electrode's cable, unless explicitly instructed or authorized by the electrode's manufacturer.
- Do not connect any devices (e.g., measurement) to the electrodes unless they have been supplied by and specifically indicated for such a use by the manufacturer.

Use of Generator (including Electrocution Hazard)
- No modification of this equipment is allowed.
- To avoid risk of electric shock, this equipment must only be connected to a supply mains with protective earth.
- The Generator internally produces voltages that are dangerous and may be fatal. The Generator does not contain parts serviceable by the User, and should not be opened.
- Do not use the Generator in the presence of flammable or explosive gas mixtures.
- For electrical safety, the Generator needs grounding. Use only medical grade main power supply cords, e.g., those supplied by the manufacturer.
- Before plugging the Generator to the main, ensure that the main power cords are not damaged. Replace them if any damage is noticed – main cords cannot be repaired.
- Do not connect or disconnect the Generator from the main power cord with wet hands.
- Confirm that the main power cord will be connected to a properly grounded electrical outlet.
- Whenever necessary, replace Generator fuses only with fuses specified in this manual.
- Maintenance should be carried out only by trained personnel. The Generator must undergo periodic preventative maintenance as specified in the Maintenance and Service.
- The NanoKnife User Manual is a fundamental part of the Generator and should always accompany it. Users must refer to this manual for correct and complete information on the use of the Generator.

Adverse Events:
Adverse effects that may be associated with the use of the NanoKnife system include, but are not limited to the following: Arrhythmia • Atrial fibrillation or flutter • Bigeminy • Bradycardia • Heart block or atrioventricular block • Paroxysmal supraventricular tachycardia • Tachycardia • Reflex tachycardia • Ventricular tachycardia • Ventricular fibrillation • Damage to critical anatomical structure (nerve, vessel, and/or duct) • Dysuria • Epididymitis • Erectile Dysfunction • Fistula formation • Haematuria • Hematoma • Hemorrhage • Hemothorax • Infection • Pneumothorax • Prostatitis • Reflex Hypertension • Unintended mechanical perforation • Urethral stricture • Urinary incontinence • Urinary retention • Urosepsis • Vagal Stimulation, asystole • Venous Thrombosis

The NanoKnife System must be operated by properly qualified personnel only.

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

Refer to Directions for Use and/or User Manual provided with the product for complete Instructions, Warnings, Precautions, Possible Adverse Effects and Contraindications prior to use of the product.

NanoKnife.com

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