



NanoKnife®
Irreversible Electroporation



ANGIODYNAMICS®

THE FIRST SURGICAL ABLATION SYSTEM BASED ON Irreversible Electroporation Technology

Cutting Edge Technology

Irreversible Electroporation (IRE) is a non-thermal, ablation technology designed for precise and effective surgical ablation of soft tissue. The NanoKnife® IRE System is the first surgical ablation system based on Irreversible Electroporation technology and represents the next generation in focal ablative therapy.

The NanoKnife IRE System enables physicians to treat otherwise difficult to treat parts of the body, near critical structures like vessels and ducts, thereby expanding the physicians' treatment options.

How NanoKnife® IRE System Works

The NanoKnife IRE System uses a series of microsecond electrical pulses to open “pores” in the cell membranes. The electrical pulses are delivered through several needle-like probes placed into or around the ablation zone under CT or ultrasound guidance. By applying enough high voltage energy, the open pores cause irreversible damage to the cells. The cells die and are removed by the human body's own lymphatic system. The procedure is done under general anesthesia and requires muscle blockade.

While other ablative modalities utilize extreme heat or cold, which can irreparably damage healthy tissue in the area, recent studies¹²³⁴⁵⁶ show that blood vessels, ducts, and other delicate anatomical structures near the ablation zone remain viable—making NanoKnife IRE System a compelling tool for difficult-to-treat parts of the body.

The Non-Thermal Advantage

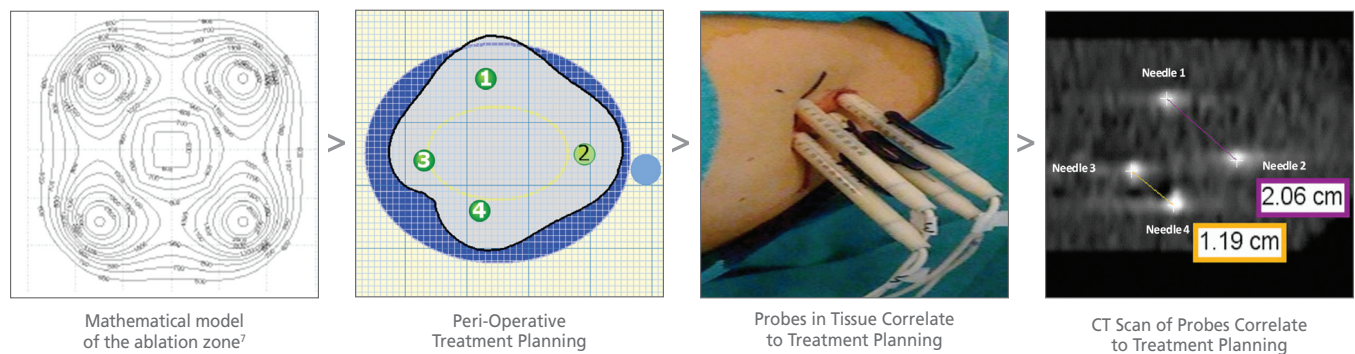


Figure 1: Following NanoKnife IRE treatment, blood vessels, ducts, and other collagenous structures in the treated area remain viable.

Irreversible electroporation, or IRE, is a generation apart from other ablation therapies that use extreme heat or cold, radiation or microwave energy. Unlike these ablative modalities, the NanoKnife IRE System is non-thermal, poses no heat sink issues and does not affect the blood vessels, ducts, and other critical structures. As a result, NanoKnife IRE System has the potential to expand the application for focal ablative therapy to include cells at or near vital structures—making NanoKnife a compelling treatment option in difficult-to-treat areas and for patients who are not candidates for surgery due to the location which requires treatment.

A New Level of Precision

Physicians have experienced challenges with other ablative modalities, such as cryoablation or microwave ablation, because these modalities are unable to provide clear, predictable ablative zones. This is not the case with the NanoKnife IRE System, which enables physicians to clearly target soft tissue within an ablation zone.



Based on a mathematical model, the NanoKnife IRE System offers a predictable ablation zone. The NanoKnife IRE System accurately correlates four phases of the procedure providing predictable ablation zones.

The proprietary treatment planning software provides a precise calculation of the tissue volume and shape that will fall within the ablation zone. All cells within the calculated ablation zone will be irreversibly porated while the collagenous structures remain unaffected.

Testimonials

"NanoKnife IRE therapy is a novel ablative modality which may allow us to treat patients who we could not otherwise treat, such as patients with locally advanced disease which is unresectable due to location. As a surgeon, I see value in utilizing IRE as an adjunct to surgery to widen my field of treatment at or near critical structures to increase resectability and/or accentuate margin."

– KEVIN T. WATKINS, M.D.

Chief, Upper GI and General Oncologic Surgery
Stony Brook University Medical Center

" NanoKnife IRE is an important new treatment modality that destroys tissue at the cellular level, enabling us to treat lesions at or near critical structures without collateral damage to blood vessels and bile ducts. With the NanoKnife IRE System, we can reach and treat lesions in difficult locations – which cannot be treated effectively with thermal ablative therapies. This allows me to offer a treatment option to some patients who have no other recourse."

– GOVINDARAJAN NARAYANAN, M.D.

Chief – Vascular Interventional Radiology
Program Director – Interventional Radiology Fellowship
University of Miami – Miller School of Medicine



THE NANOKNIFE® IRE SYSTEM BENEFITS:

Unlike other ablative modalities, NanoKnife IRE System has the potential to expand treatment options available for patients who are not candidates for surgery due to the location which requires treatment.

Additional benefits include:

- **Non-thermal**
 - High voltage pulses permanently open pores in target cell membranes
 - Eliminates heat sink issues
 - Ablate at or near vital structures (e.g., blood vessels, bile ducts, other tissues containing collagen/elastin)
- **Potential to spare critical structures—vasculature and ducts remain intact**
- **Ablated tissue removed by the body's natural processes within weeks**
 - Mimics natural cell death
- **Allows real-time CT/US imaging of ablated zones**
- **Minimal to no post-procedural pain compared to other traditional modalities**

¹ Lee et al, Irreversible electroporation (IRE) eradicating rabbit VX2 liver tumor, UCLA Medical Center, SIR 2010 Abstract

² Hwang et al, Safety of irreversible electroporation in the pancreas: Pre-clinical assessment in the porcine pancreas, Stanford University, SIR 2010 Abstract

³ Guo et al, Liver directed irreversible electroporation therapy: Longitudinal efficacy studies in a rat model of hepato cellular carcinoma, Northwestern University, SIR 2010 Abstract

⁴ Deobar et al, Irreversible electroporation in swine kidney: radiological pathological correlation, Memorial Sloan Kettering, SIR 2010 Abstract

⁵ Deobar et al, Irreversible electroporation in swine lung: radiological pathological correlation, Memorial Sloan Kettering, SIR 2010 Abstract

⁶ Charpentier et al, Irreversible electroporation of the liver and liver hilum in swine, Rhode Island Hospital and Warren Alpert School of Medicine, SSO 2010 Poster

⁷ Rubinsky, B., Onik G., Mikus, P. "Irreversible Electroporation: A New Ablation Modality - Clinical Implications." Technology in Cancer Research and Treatment, Vol 6 No 1, pp 37-48, 2007.

IMPORTANT RISK INFORMATION

INDICATION FOR USE: The NanoKnife® IRE System with six outputs is indicated for surgical ablation of soft tissue. The system includes an energy generator, footswitch and single-use disposable electrodes.

CONTRAINDICATIONS: Procedures based on high voltage pulses are not recommended in the following cases: Treatment of lesions in the thoracic area in the presence of implanted cardiac pacemakers or defibrillators; treatment of lesions in the vicinity of implanted electronic devices or implanted devices with metal parts; treatment of lesions of the eyes, including the eyelids; or patients with a history of Epilepsy, cardiac arrhythmia, or recent history of myocardial infarction. The effects of NanoKnife IRE System use on a fetus are

not known. Procedure on pregnant women should be contemplated only after ensuring that the procedure benefits outweigh the risks.

WARNINGS AND PRECAUTIONS: CAUTION: Federal (USA) law restricts the sale of this device by or on the order of a physician. The electrodes are sterilized by ethylene oxide and intended for single patient use. Sterile unless the package is opened or damaged. Do not re-sterilize or use if the device's insulation is damaged. Avoid short-circuiting the electrodes when delivering pulses. The device is intended for use with an AngioDynamics irreversible electroporation generator only. NanoKnife Generator: Caution – Electrocution Hazard! The Generator internally produces voltages that

are dangerous and may be fatal. Do not use the Generator in the presence of flammable or explosive gas mixtures. Do not use the Generator if a malfunction is suspected. The physician MUST read the User Manual thoroughly before operating the NanoKnife System.

POTENTIAL COMPLICATIONS: Dissection, perforation, hemorrhage, hematoma, or infection.

Indications, contraindications, warnings and instructions for use can be found in the Instructions for Use supplied with each NanoKnife electrode probe and system. Observe all instructions prior to use. Failure to do so may result in patient complications. CAUTION: Federal (USA) law restricts the sale of this device by or on the order of a physician. This device is sterilized by ethylene oxide. The electrodes are intended for single patient use only.

ANGIODYNAMICS®

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The NanoKnife IRE System is cleared by the U.S. Food and Drug Administration for surgical ablation of soft tissue.
The NanoKnife IRE System also contains the CE mark and is available in Europe.