



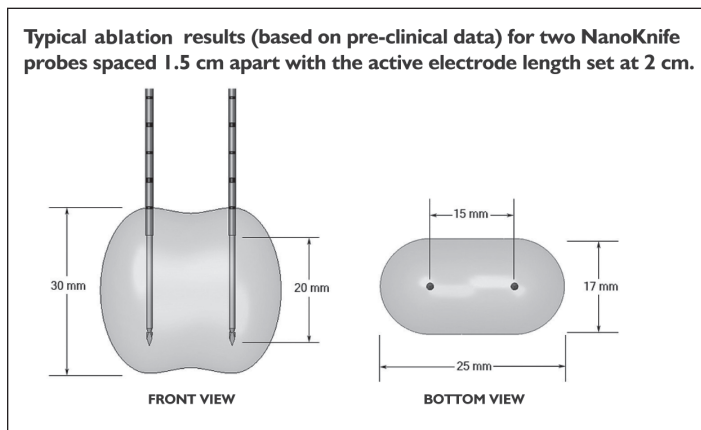
Irreversible Electroporation and the NanoKnife™ System

A New Ablation Technology

Irreversible Electroporation (IRE) is a surgical ablation technique in which electrical fields are used to create nano-scale defects in a cell's membrane, which causes cell death only in targeted tissue, while critical structures such as ducts, blood vessels and nerves remain functional.

The NanoKnife IRE surgical ablation system is the first to use irreversible electroporation to treat soft tissue lesions. Two or more single electrode probes, or one bipolar probe, are positioned in or around the lesion and an electrical field is created between them in a series of micro-second pulses, which induces cell death in the encompassed soft tissue. Unlike cryo-ablation or radiofrequency ablation, which use thermal treatments to destroy tissue, IRE treats without exposing tissue to extreme cold or heat, eliminating a major cause of treatment failure and possible damage to normal tissue. IRE treats similar volumes of tissue to RFA and cryo surgery, typically in a fraction of the time; less than four minutes for a four by three centimeter volume.

IRE treatment using the NanoKnife system is minimally invasive, and is performed under general anesthesia with ultrasound or CT guidance. Pre-operative imaging allows precise calculation of the tissue volume and shape to be treated, and aids the planning of appropriate positioning for the NanoKnife IRE electrodes. The IRE treatment consists of a series of ninety extremely short electrical pulses, each less than 100 millionths of a second. Cell death is induced within seconds, and the IRE procedure is normally completed in just minutes.



The IRE treatment using the NanoKnife system induces cell death in soft tissue only. NanoKnife™ electrodes are placed in proximity to the targeted lesion, but – unlike thermal ablation technologies –

surrounding critical structures including nerves and blood vessels remain functional. During treatment, the unique action of the NanoKnife™ System opens permanent nano-sized pores in the cell membrane, causing irreversible damage which rapidly induces a natural cell death. After IRE treatment, cells that form the nerves, blood vessels, and other collagenous tissues in the treated area remain viable, reducing the risk of damage to these structures. Microscopic imaging after treatment reveals a sharply delineated separation between affected and unaffected cells.

The treated area begins to resolve immediately after the procedure, as the body's normal healing response produces cells that engulf and remove treated cells from the region, much like the healing process of a bruise. Doppler ultrasound imaging during ablation demonstrates the patency of blood vessels, as small as one millimeter in diameter in the treated area. Thirty days after NanoKnife surgical ablation, CT and ultrasound imaging reveal a mostly normal appearance, with little remaining evidence of the IRE treatment. As seen on imaging, critical structures continue to function normally; blood flow in the treated area aids healing and minimizes potential treatment side-effects.

NanoKnife Generator Specifications

Number of Probe Outputs	1 - 6
Number of Pulses*	90
Pulse Amplitude	100 to 3000 V
Pulse Length	20 - 100 μ Sec
Pulse Amplitude Precision	\pm 5%
Pulse Length Precision	\pm 2 μ Sec or 2%
Maximum Current	50 A

* Number of pulses for each pair of electrodes.

A research team based primarily at the University of California, Berkeley, invented the IRE technology that is now being used in the NanoKnife platform by physicians. The technology was exclusively licensed by the University of California to a company named Oncobionic for commercial development. With the close of the acquisition of Oncobionic in April 2008, AngioDynamics has taken ownership of the exclusive license along with a developing portfolio of intellectual property around IRE. In the United States, NanoKnife has been cleared by the FDA for use in the surgical ablation of soft tissue.

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