NanoKnife® – An Introduction

Minimally invasive tissue ablation has become of central importance in the modern surgery armamentarium. In the treatment of benign or malignant tumors it is important to achieve ablation of the undesirable tissue in a well-controlled and precise way without affecting the surrounding healthy tissue. As an alternative to surgical resection, a number of minimally invasive methods have been developed to destroy specific areas of undesirable tissues. Most of these techniques are thermal using cold, e.g. cryosurgery or heat, e.g. radiofrequency.

Electroporation, also known as electropermeabilization, is a term used to describe the permeabilization of the cell membrane as a consequence of the application of certain short and intense electric fields across the cell membrane, the cells or the tissues. The permeabilization can be temporary (reversible electroporation) or permanent (irreversible electroporation) as a function of the electrical field magnitude and duration, and the number of pulses. Reversible electroporation is commonly used in vitro to facilitate the penetration of various otherwise non-permeable macromolecules across the cell membrane. Irreversible electroporation, the ability of certain electrical pulses to permanently permeabilize the cell membrane, has been known for over three decades. For most of this period irreversible electroporation (IRE) was used primarily for ablation of microorganisms and cells in vitro and studied only as an upper limit of electrical parameters for reversible tissue electroporation applications. AngioDynamics has pursued the understanding of the electrical fields and processes that produce IRE with single cell micro-electroporation technology.

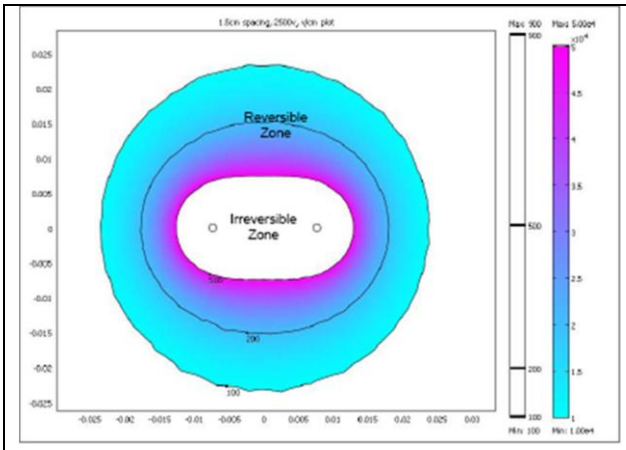
NanoKnife® Therapy: What is it?

- A new focal ablation therapy that uses low energy electrical pulses to permanently open pores in the cell membranes of soft tissue, which causes cells to die.

- Uses high voltage, but low energy direct current (LEDC) – and does not rely on heat to create the tissue effect. This allows physicians to treat soft tissue near critical structures, like blood vessels, ducts, or lymph nodes.

- Well-suited for patients who have non-resectable soft tissue disease near critical structures and who otherwise have no other treatment option given the location of their disease.

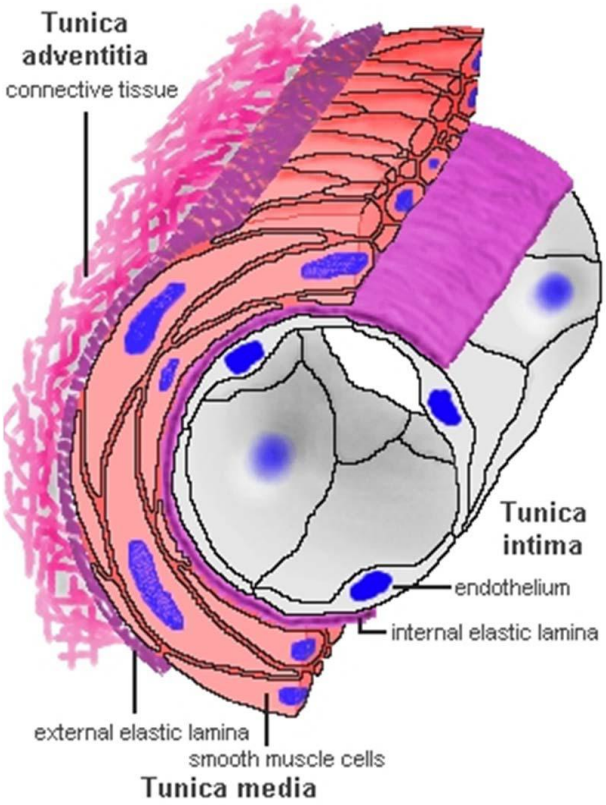
How NanoKnife® Technology Works



- Rapid series of short, electrical pulses
- Low energy direct current (LEDC).
- High voltage, but low energy
- Ablation effect is not thermal
- Nano-sized defects (“pores”) created in cell membrane.
- Cell death occurs (mimics natural cell death).
- Resulting debris eliminated through vascular pathways.

Notes:
• White zone represents irreversible electroporation.
• Diagram developed from a mathematical model.

Cellular vs. Non-cellular Tissue Affects

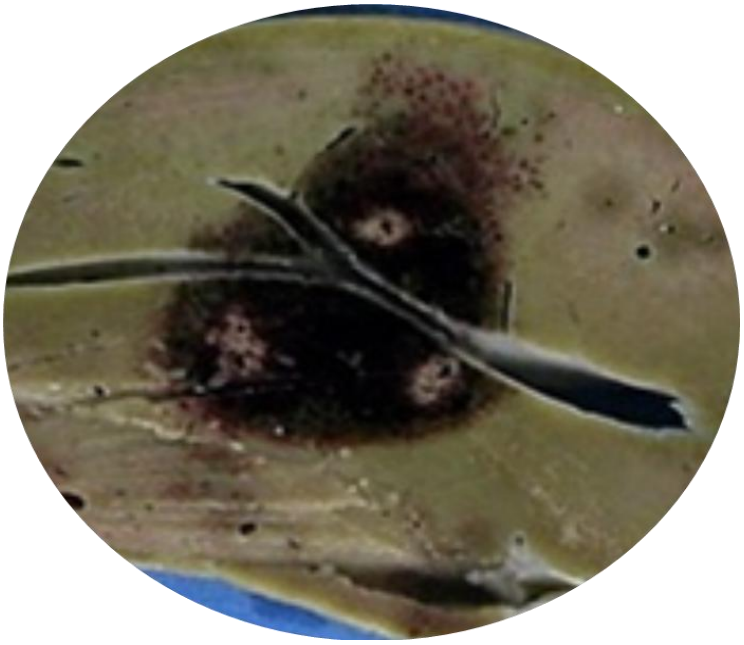


All *cells* in ablation zone are irreversibly porated

Collagenous structures are not affected

- Intact adventitia & laminae visible at 2 days with no smooth muscle cells present
- Endothelium largely repopulates at 2 days
- Smooth muscle repopulated at 2 weeks

No Heat Sink Effect



NanoKnife®: Clinical Advantages:

- Uses high voltage, low energy electrical pulses to achieve tissue effect
  - not a thermal therapy
  - Eliminates heat sink issues
  - Provides ability to ablate soft tissue at or near critical structures (e.g., blood vessels, bile ducts, other tissues containing collagen/elastin)

- Provides 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)

- Provides predictable zone of ablation (treatment area)

- Allows real-time CT/US imaging of ablated zones

- Patients report experiencing minimal to no post-procedural pain

NanoKnife: Where is it used?

Inoperable tumors of:

- Liver
- Pancreas
- Prostrate
- Lung
- Kidney

Tumors that are close to critical structures

NanoKnife® System

- The NanoKnife System consists of the generator (pictured at right), footswitch, power cord, and a line of single-use disposable electrodes.

System has:

– Up to 6 outputs with programmable, automatic switching between each output.
– USB port to download patient data.

- FDA 510(k) clearance for the surgical ablation of soft tissue.

- System also carries the CE mark.

NanoKnife®

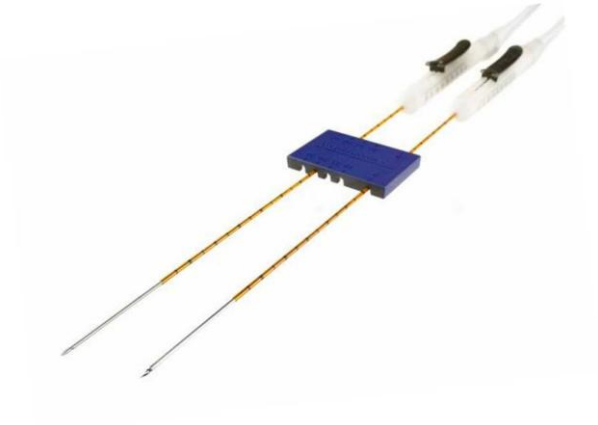
Monopolar Electrode

- Single Electrode
- Disposable
- 15 cm length
- 25 cm length
  – When insufflation is used
  – Obese patients

Monopolar Electrode

Key Features

- 19 gauge needle with depth markings
- Echogenic needle surface
- Active electrode length adjustable in 0.5 cm increments from 0 – 4 cm
- Maximum insertion depth – 15 cm
- 8 foot connection cable



Support:

- Hands on training and observation visit would be arranged for one doctor.

- A product specialist would be available to assist the doctor for the first 2 cases.