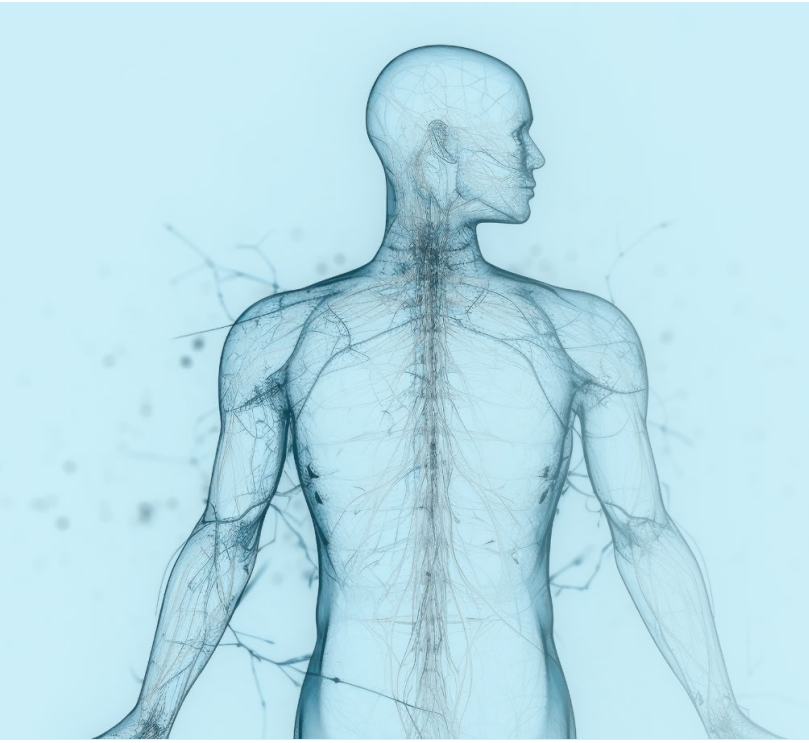


Pulse Biosciences®

Powering the next generation in bioelectric medicine for Minimally Invasive Surgery with **Nanosecond Pulsed Field Ablation** technology.

Indications for Use: The CellFX Percutaneous Electrode System is indicated for ablation of soft tissue in percutaneous, and intraoperative surgical procedures. The CellFX Percutaneous Electrode System (Percutaneous Electrode) is not indicated for use in cardiac procedures.

The CellFX Percutaneous Electrode System is FDA Cleared for use in the United States only.

Pulse Biosciences, Inc.

- Launched in 2015 with Over 15 Years of University and Industry Research and a Broad IP Portfolio
- Inventors and Sole Manufacturers of the CellFX® System, A Novel and Proprietary nsPFA™ Platform for Use Across Multiple Applications
- FDA Cleared and CE-Mark Technology with Proven Results on Over 6,000 Patients with No Serious Adverse Events
- Unique Bioelectric Mechanism of Action with Game-Changing Soft Tissue and Cardiology Applications

Pulse Biosciences®

The Journey from nsPFA Concept to Clinical Applications

Original Research into Nanosecond Pulsing by Karl Schoenbach
1985-1995

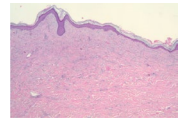
First paper showing nsPFA can reduce tumor growth
2002

Nanosecond PFA Company Pulse Biosciences Formed
2014

First nsPFA Clinical System
Aug 2016

Health Canada
Jun 2021

CE
Jan 2021

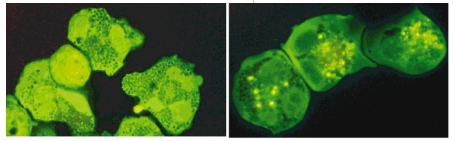


Basal Cell Carcinoma Study
2022

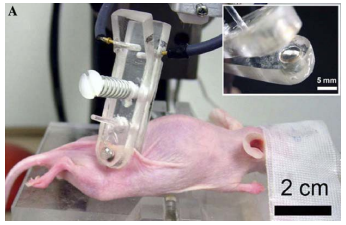
FDA Clearance Percutaneous Ablation
March 2024

1985-1994 | 1995 | 2001 | 2002 | 2006 | 2014 | 2016 | 2019 | 2021 | 2022 | 2023 | 2024

First Nanosecond Pulsed Field Generator
1995



First direct proof that nsPFA penetrates cytoplasm Schoenbach, Beebe and Buescher "Intracellular effect of ultrashort electrical pulses"
2001



First paper showing nanosecond pulses cause melanomas to self-destruct
2006

Prototype Generator
Jan 2016

First nsPFA Commercial System
2019

FDA
Feb 2021

Thyroid First-In-Human Study
2023

Pulse Biosciences®

Evolution of CellFX® Technology

nsPFA energy + devices optimized for nsPFA and application = differentiated clinical results

nsPFA ENERGY

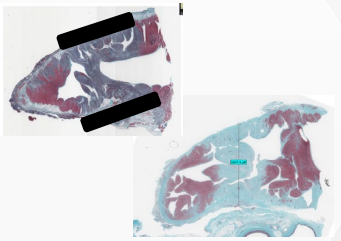
Nanosecond pulses induce regulated cell death while sparing vital acellular structures

CELLFX CONSOLE

Commercial-ready, proprietary, tunable platform applies customized treatment parameters for differentiated end-effectors

SCIENTIFIC KNOWLEDGE

CellFX technology is backed by extensive preclinical and clinical studies, and commercial use in dermatology



CLINICAL APPLICATIONS

Devices optimized for each application offer a complete streamlined solution

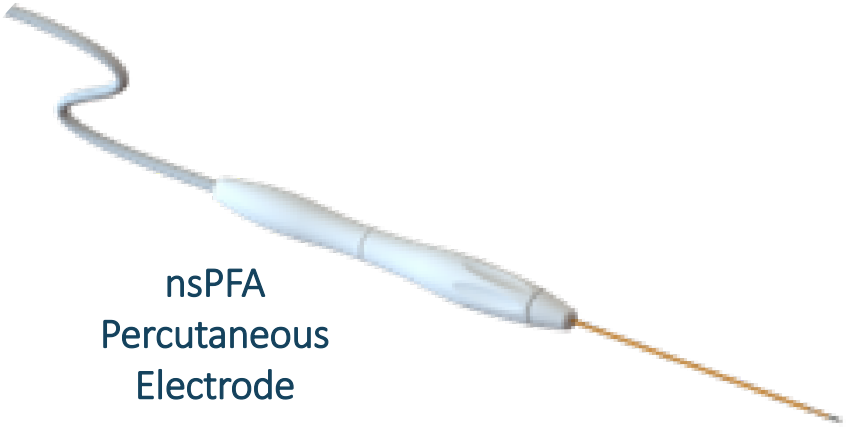
Pulse Biosciences®

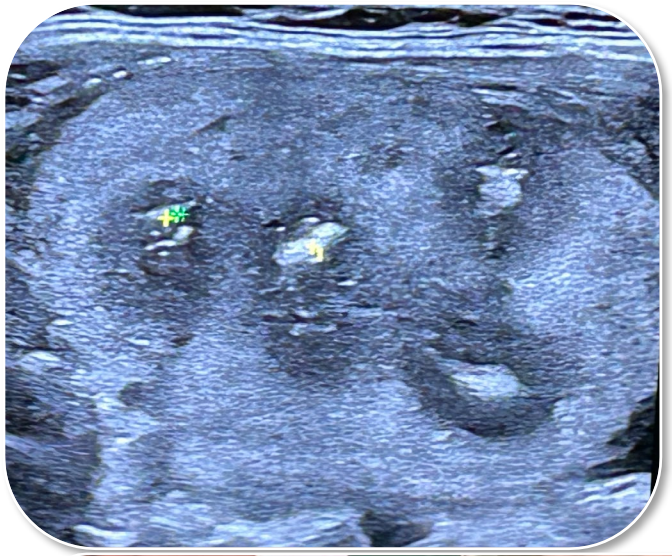
CellFX® nsPFA Percutaneous Electrode System™

Nonthermal ablation for improved nerve safety, quicker resolution, and no scar/necrotic ball formation

nsPFA Console

nsPFA Percutaneous Electrode





- 8 second ablation cycles for a quicker procedure, no moving-shot technique required
- Regulated cell death MOA results in improved healing response
- Nonthermal mechanism is safe near critical structures, enables quick resolution (~30d), without necrotic ball formation

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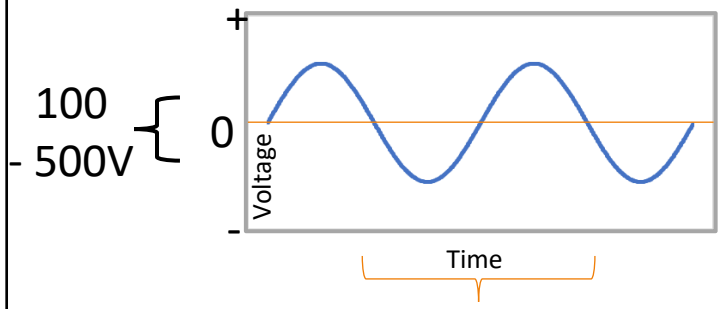
Therapeutic Electrical Energy Modalities

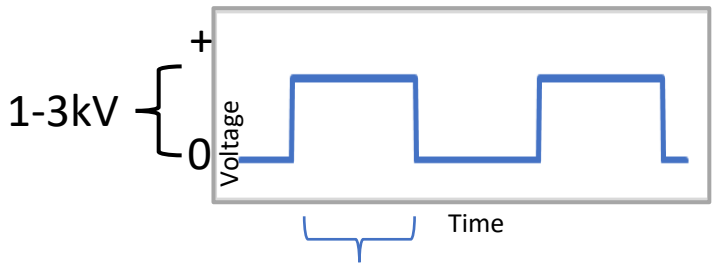
Radiofrequency
(Radiowave spectrum)



Microseconds (millionths)

- Alternating current (AC)
- Heats tissue by electrical resistance
- Damage is thermal and non-selective
- Dominant manner of injury: thermal, immediate necrosis

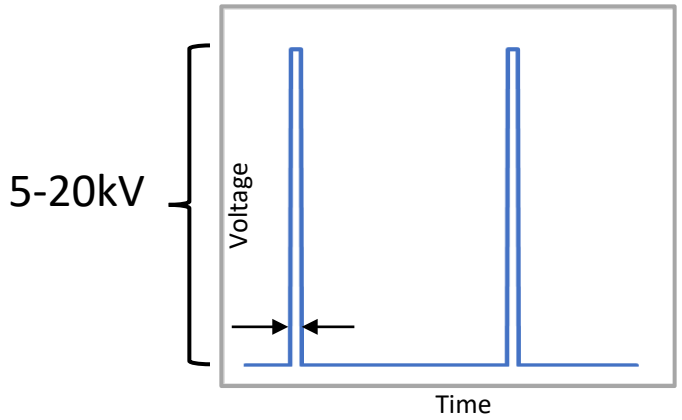
Irreversible Electroporation
(Microsecond pulsing)



Microseconds (millionths)

- Direct current (DC)
- Electrical field effect
- Destroys cell membranes
- Damage is selective for cellular structures
- Dominant manner of injury: traumatic, immediate necrosis
- Significant muscle/nerve stimulation

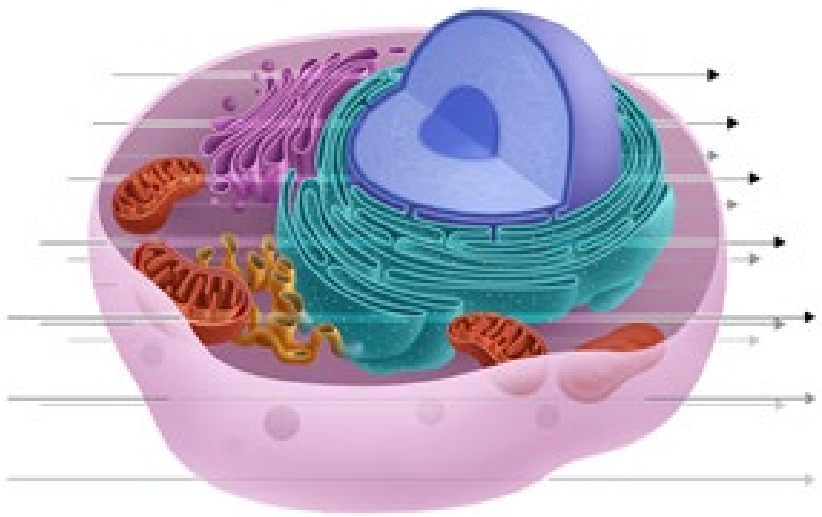
Nanosecond Pulsed Field Ablation
(Nanosecond Pulsing)



Nanoseconds (billionths)

- Direct current (DC)
- Electrical field effect
- Damages cell organelles.
- Damage is selective for cellular structures
- Dominant manner of injury: atraumatic, regulated cell death (like apoptosis)
- Minimal muscle/nerve stimulation

What is Nanosecond Pulsed Field Ablation (nsPFA)?



- Creates a high-voltage DC electric field in very short-duration pulses
- Penetrates the cell membrane and disrupts internal cellular function, leading to regulated cell death
- Eliminates targeted cells while sparing adjacent noncellular tissue
- Nonthermal treatment – because total energy delivered is low

Proprietary nsPFA Energy Provides Unique Mechanism of Action

Stimulates natural and precise Regulated Cell Death (RCD) in any cell without collateral damage

Nonthermal modality that delivers nanosecond duration pulses of electrical energy

High speed nanosecond energy pulses penetrate the cell membrane and disrupt internal cellular function, leading to **Regulated Cell Death (RCD), akin to Apoptosis**

Unlike thermal (heat/cold) modalities, nsPFA directly impacts cellular structures while sparing noncellular tissue (including collagen, vessels, and nerves)

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Proprietary nsPFA Mechanism of Action Video

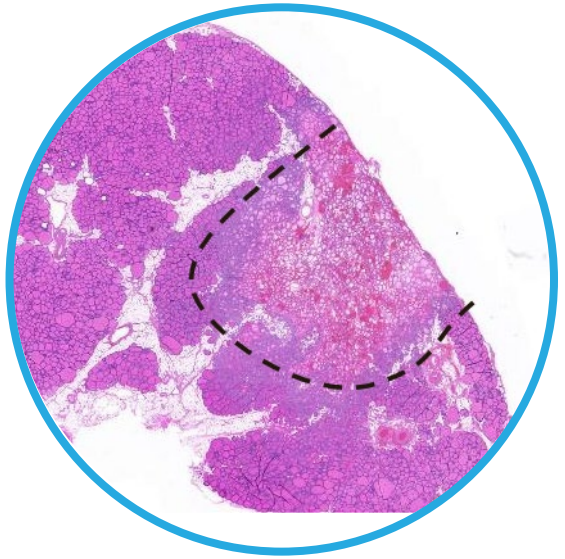
Pulse Biosciences®

Click to Open Video Link

Percutaneous Delivery of nsPFA Energy – Thyroid

nsPFA Console

Proprietary nsPFA-Optimized Percutaneous Needle Design



2-day Post NPS-treated thyroid (1x, H&E) showing loss of differentiation

- Rapid ablation of thyroid tissue with ablation zones of up to 3cc / shot in 8 seconds[1]
- Single treatment efficacy with 100% clearance within ablation zone in less than 90 days[1]
- Extremely reduced risk of nerve and esophageal injury due to short-duration nsPFA pulses[1]
- Preclinical and clinical data demonstrating safe, fast and effective ablations[1]

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1) Data on File.

Procedure Overview: Ablation of Thyroid Nodules with the nsPFA Percutaneous Electrode

Insertion of percutaneous electrode using ultrasound guidance and local anesthesia

Needle tracks can be visualized under ultrasound imaging because of electrolysis bubbles forming on electrodes

Procedural Steps

1. Lidocaine injection with standard technique
2. nsPFA electrode is inserted into distal portion of the nodule
3. Ablation cycle is initiated using a stationary technique (no moving shot)
4. nsPFA electrode is retracted and positioned for next ablation, overlapping slightly
5. Ablation cycles are repeated throughout length of needle track
6. nsPFA electrode is reinserted as needed to treat full nodule

Ablation Characteristics[1]

- Each ablation cycle is delivered in 8 seconds
- Two energy settings for procedural flexibility
- Each ablation volume is approximately 1.5cm x 1 cm
- Ablation of a full nodule takes about 5-20 minutes, depending on nodule size

Pulse Biosciences®

1) Data on File.

Thyroid Clinical Feasibility Study

Objective:

A feasibility study to evaluate safety and efficacy of the nsPFA Percutaneous Electrode for thyroid ablation

3 Groups:

- Treat and resect (N=5) to examine histology and by ultrasound
- Percutaneous ablation of 2-4 isolated areas to characterize ablations (N=20)
- Full nodule ablation (N=5)

Key Findings and Observations:

- No reported serious adverse events (SAEs)
- Electrode and treated areas visualized on ultrasound
- Majority of reduction of treated areas in first 30 days
- No appearance of scarring or fibrosis on follow-up ultrasound

Presented at North American Society of Interventional Thyroidology 2024
By Prof. Stefano Spiezia

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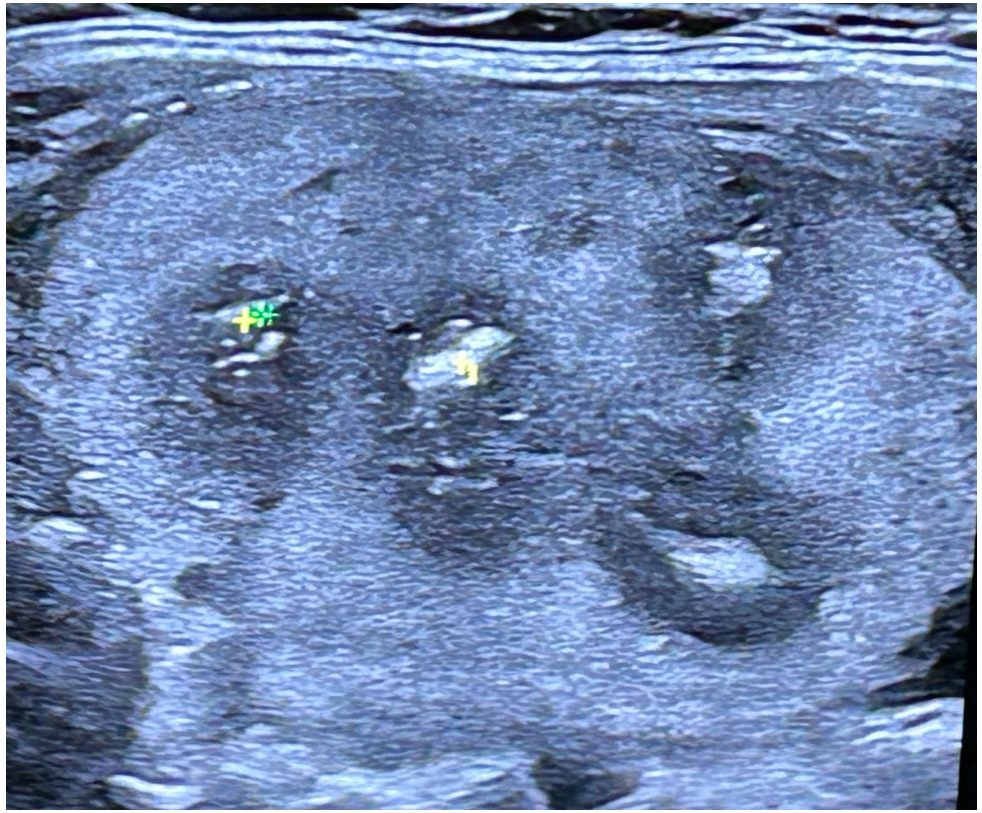
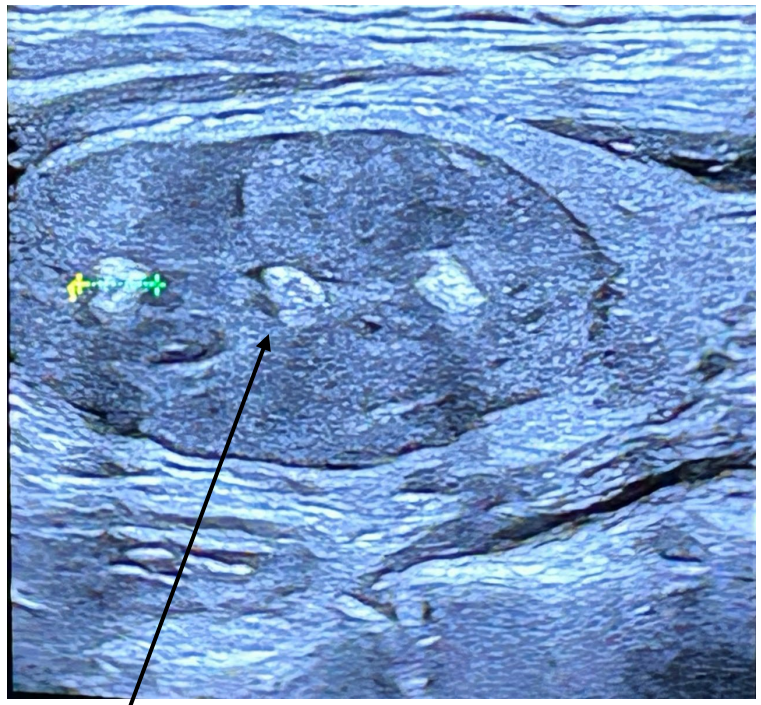
Intraoperative Visualization of Ablation Zones

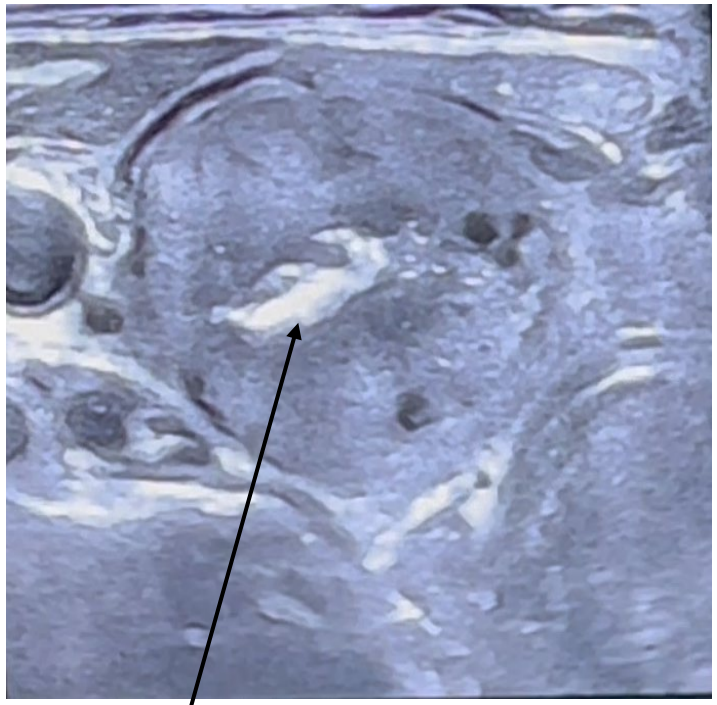
Hypoechoic Ablation Zones



Needle tracks can be used for navigation



Able to place 3 ablations in a straight line equidistant apart.



Along the needle track.

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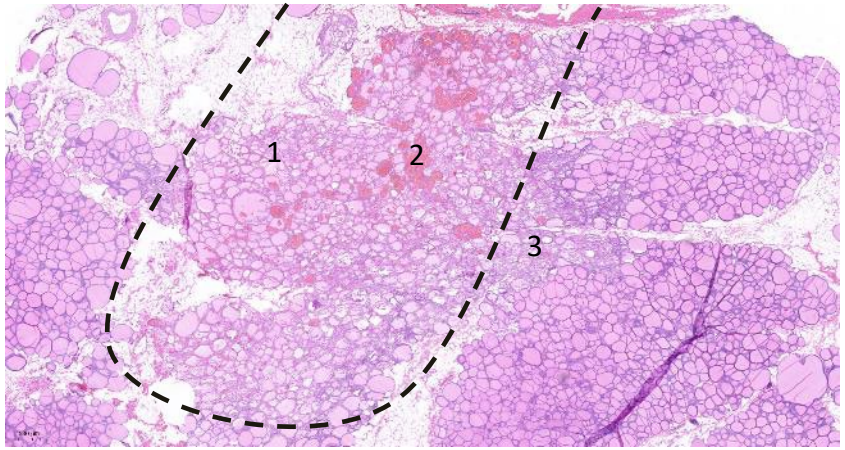
Thyroid Clinical Feasibility Study Conclusions from Dr. Spiezia

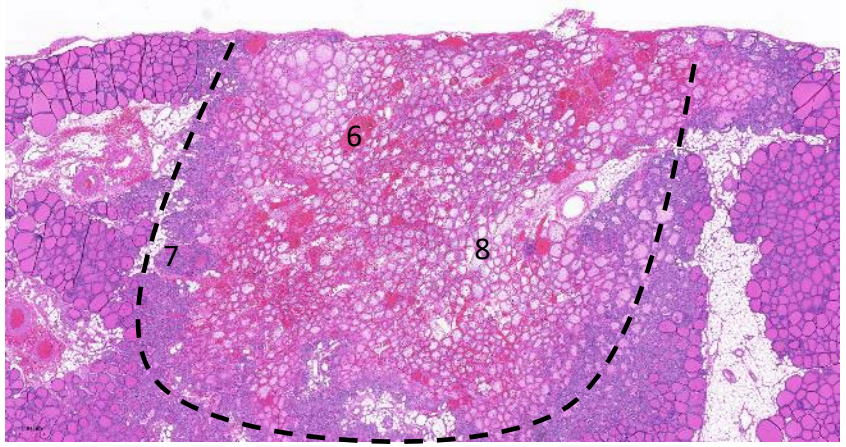
Conclusions and Clinical Implications

- The nsPFA percutaneous electrode created ultrafast, consistent ablations in benign thyroid nodules with a fixed technique, with no reported SAEs, supporting the clinical feasibility of this new modality
- The nonthermal nature of nsPFA spares surrounding acellular tissues and can be used in a variety of tissue morphologies, including cystic and vascular nodules
- The absence of postprocedural fibrosis or scarring in the treated zones under ultrasound could improve post-procedure diagnostic clarity and overall volume reduction
- Further studies are needed to further characterize nodule resolution and post-procedural healing, with the intent to maximally ablate thyroid nodules

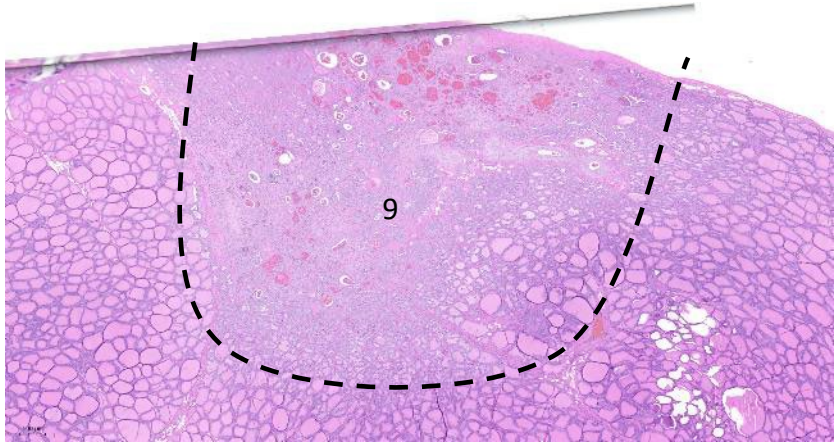
Thyroid Nodule Treatment in Porcine Study



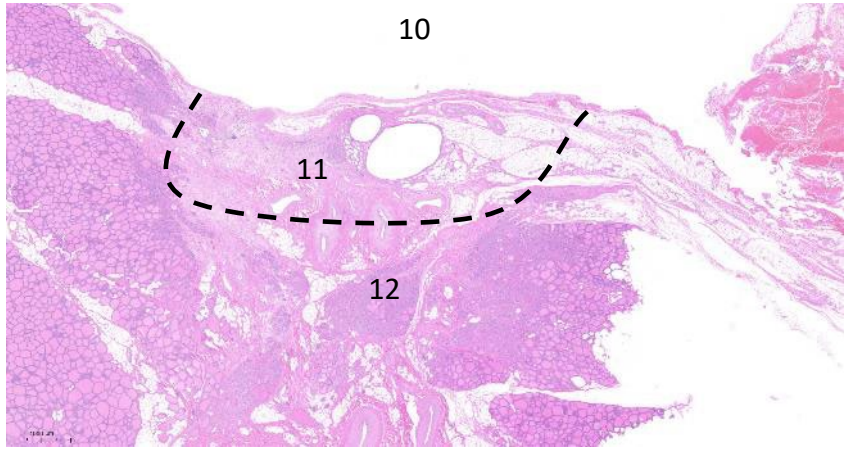
Acute (7 Hours): (2x, H&E) Loss of differentiated staining in treatment zone which coincides with region of RCD onset (1), mild hyperemia with extravasated red blood cells (2), and minimal inflammation (3). Dashed line indicates treatment zone.



2-day: NPS-treated thyroid (2x, H&E) showing mild hyperemia (6), mild inflammation (7), and dead or dying cells (8) within treatment zone. Dashed line indicates treatment zone.



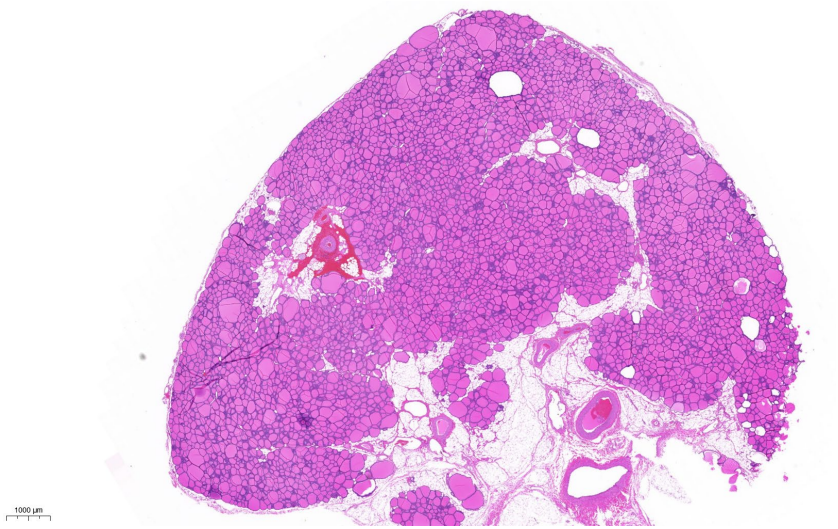
8-day: NPS-treated thyroid (2x, H&E) showing minimal inflammation that mostly consists of macrophages (9) clearing dead cells. Dashed line indicates treatment zone.



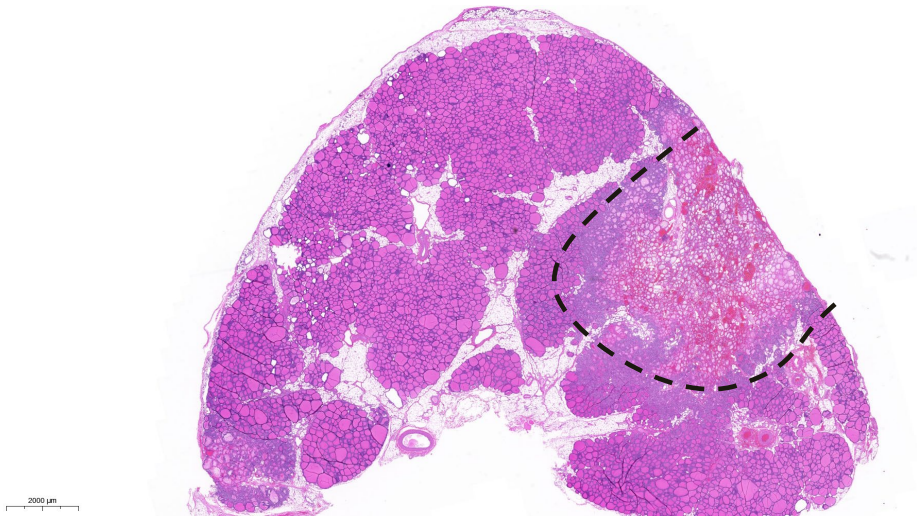
30-day: NPS-treated thyroid (2x, H&E) showing collapse of treatment zone (10), collagen synthesis and deposition (11), and continued macrophagia (12).

Porcine Thyroid Nodule Treatment: Treatment Zone Collapse

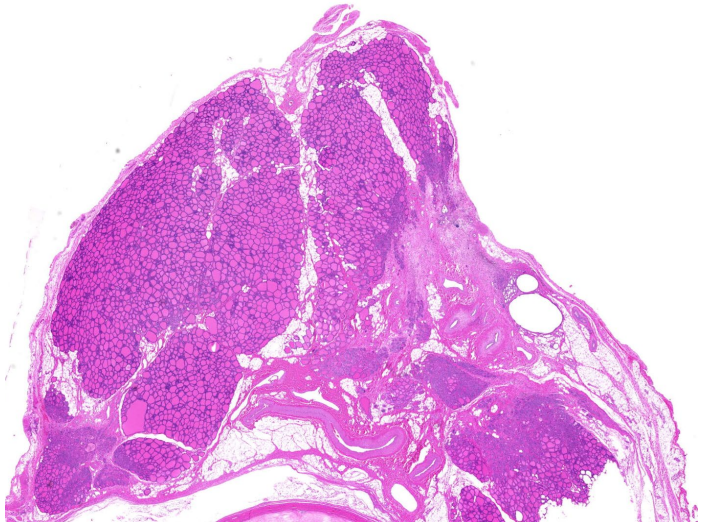
Parenchymal collapse and a reduction in tissue volume observed at 30 days post treatment



Untreated: Thyroid tissue (1x, H&E) shown for reference.

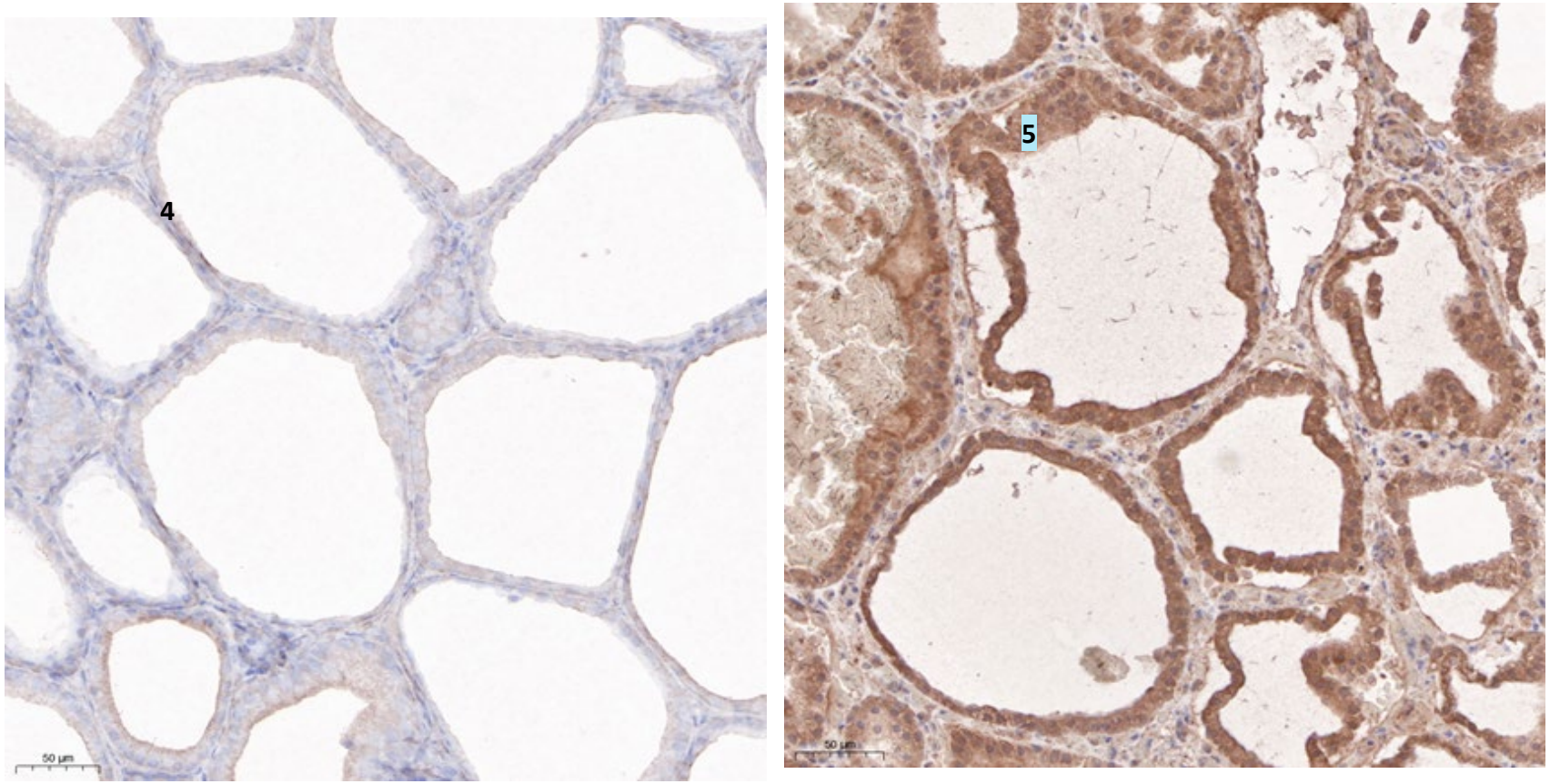


2-day: NPS-treated thyroid (1x, H&E) showing loss of differentiation, indicating dead or dying cells within treatment zone (dashed line)



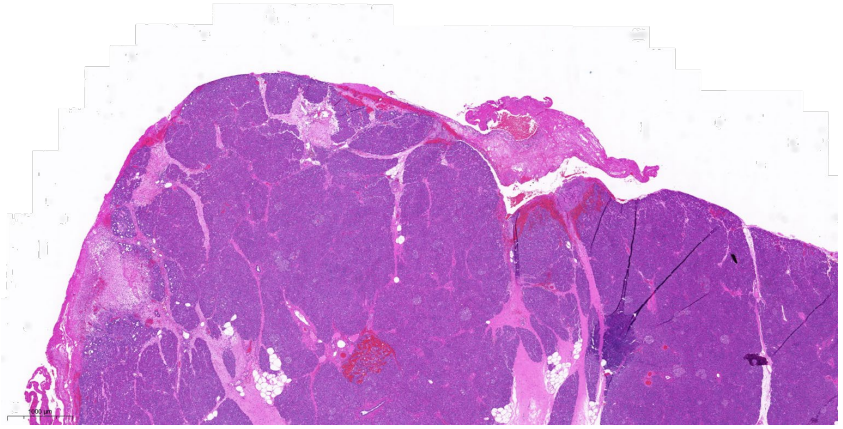
30-day: NPS-treated thyroid (1x, H&E) showing collapse of treatment zone.

Clear Evidence of RCD at 7 Hours in Porcine Model

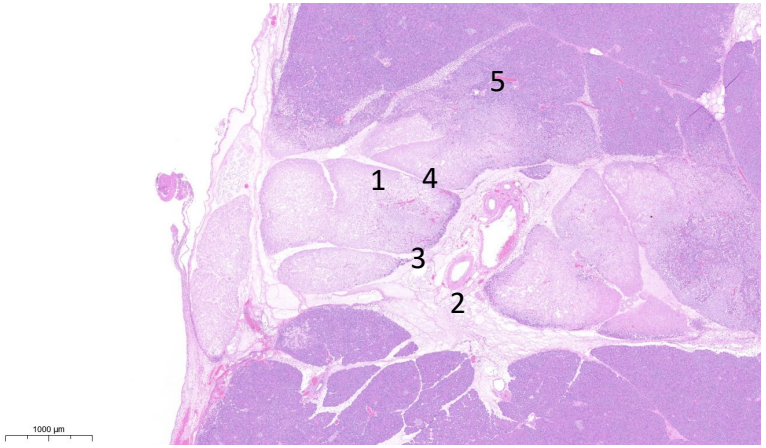


Acute (7 Hours): NPS-treated thyroid (20x, IHC) showing negative caspase 3 staining outside treatment zone (4) compared to positive caspase 3 inside (5), signaling that RCD has been initiated.

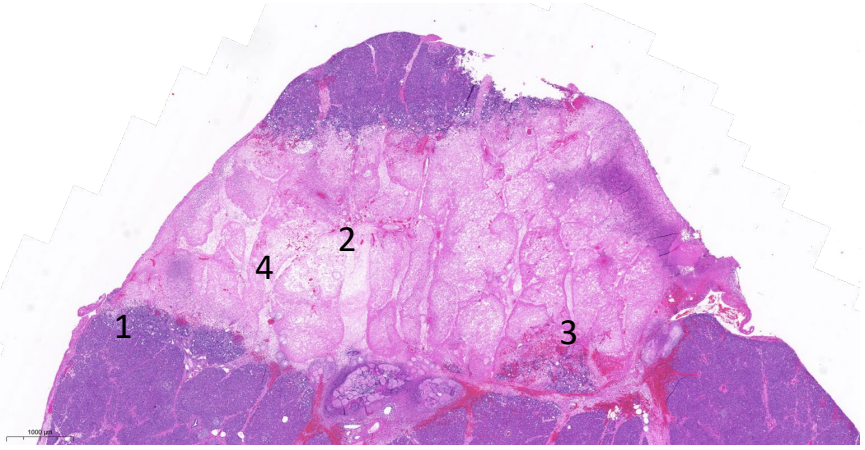
CellFX nsPFA Histology in Porcine Pancreatic Tissue



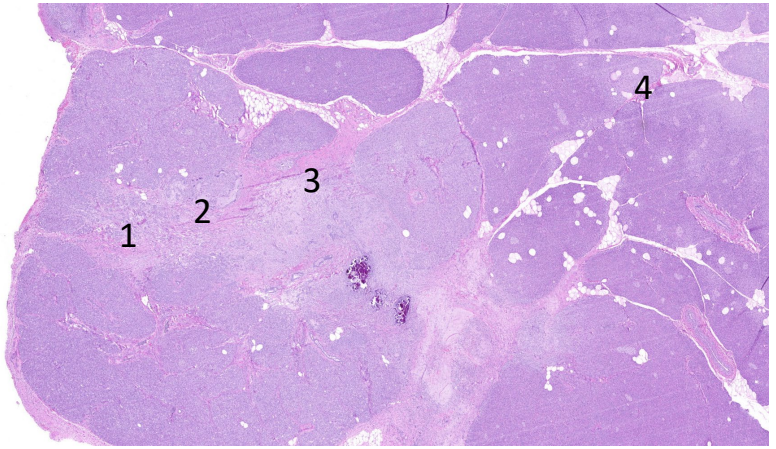
Untreated: Normal pancreatic tissue is defined by a well-developed lobular arrangement of highly cellular glandular tissue. Contains minimal collagenous connective tissue outside of the periphery of ducts. Islets of neuroendocrine cells are dispersed throughout the tissue.



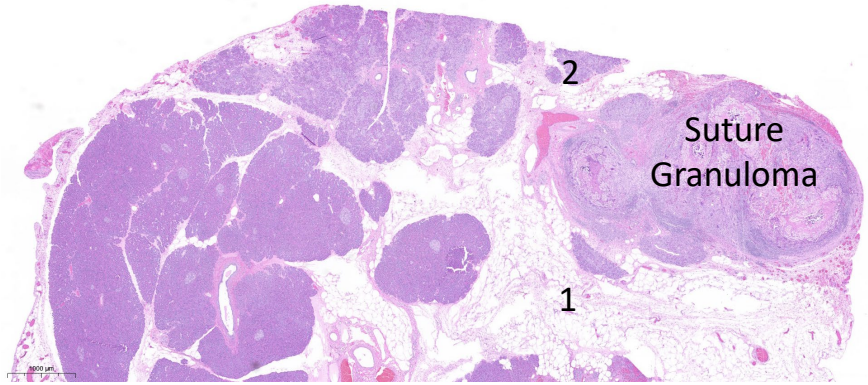
Acute (5 Hours) : Significant lytic necrosis (1) with early signs of saponification (fat breakdown) (2) and small vessel damage with RBC leakage (3) suggesting enzyme leakage, common after pancreatic cell death (4). Robust neutrophil infiltration (5) up to the necrotic lysis zone. RCD can't be determined due to rapid onset of lytic necrosis.



Day 2: Lytic necrosis lesion more mature with fewer neutrophils and clearly bounded within the treated area. Ductal hyperplasia and reorganization (1) seen near the necrotic zone. Increased fibrin (2), and red blood cell (3) leakage due to small vessel injury. Fat saponification observed (4)



Day 7: Lytic necrosis is associated with loss of pancreatic glandular structures (1). Some inflammatory cells in areas of hypercellularity near areas of lobe clearance(2). Moderate fibrosis (3) limited to areas between cleared lobes in the treated zones is observed. Evidence of saponification (4) throughout the treatment zone.



Day 30: Slightly increased cellularity in interlobular fat may suggest inflammatory response (1). Very little if any fibrosis observed. Treatment area organized into slightly smaller lobular structures compared to untreated tissue (2). Treated tissue largely cleared with little to no remaining fibrosis and no scarring present.

Pulse Biosciences®