LABORATORY INVESTIGATION

# Thermal Energy During Irreversible Electroporation and the Influence of Different Ablation Parameters

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## ABSTRACT

**Purpose:** Irreversible electroporation (IRE) uses high-voltage electric fields to achieve cell death. Although the mechanism of IRE is mainly designated as nonthermal, development of secondary Joule heating is inevitable. The study purpose was to gain understanding of temperature development and distribution during IRE.

**Materials and Methods:** IRE was performed in a transparent polyacrylamide gel resembling soft tissue. Mechanical effects, changes in temperature gradient, and absolute temperature changes were measured with three different optical techniques (high-speed, color Schlieren, and infrared imaging) to investigate the effect on temperature of variations in voltage, pulse length, active tip length (ATL), interelectrode distance, electrode configuration (parallel, convergent, and divergent), and sequential pulsing (pulse delivery interrupted by breaks). The total delivered energy was calculated.

**Results:** A temperature gradient, starting at the tips of both electrodes and expanding toward each other, developed immediately with pulse delivery. Temperatures increased with increasing voltage (by 2.5°C–40.4°C), pulse length (by 5.3°C–9.8°C), ATL (by 5.9°C–17.6°C), and interelectrode distance (by 7.6°C–21.5°C), in accordance with higher energy delivery. Nonparallel electrode placement resulted in heterogeneous temperature distribution with the peak temperature focused in the area with the shortest interelectrode distance. Sequential pulse delivery significantly reduced the temperature increase compared with continuous pulsing (4.3°C vs 11.7°C).

**Conclusions:** Voltage, pulse length, interelectrode distance, ATL, and electrode configuration each have a strong effect on temperature development and distribution during IRE. Sequential pulsing reduces the extent and volume of thermal distribution and may prove beneficial with respect to procedural safety.

## ABBREVIATIONS

ATL = active tip length, IRE = irreversible electroporation, ROI = region of interest

Irreversible electroporation (IRE) is increasingly used for the ablation of malignancies, particularly tumors located near vulnerable structures such as bile ducts and blood vessels. The technique uses high-voltage microsecond electrical pulses applied through adjustable needle electrodes. The electrical pulses are proposed to destabilize the existing cellular transmembrane potential, leading to the formation of so-called nanopores in the cellular membrane. In theory, because of the resulting increased cell membrane permeability, the cell loses its homeostatic properties, resulting in cell death (1). Because the IRE mechanism induces cell death by affecting the cellular membrane, cells are killed in a targeted region, without damage to the collagen and other interstitial tissue constituents. Critical structures

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like major vasculature and ductal systems may therefore be preserved (2,3). The sparing of critical structures is the primary characteristic that distinguishes IRE from other local therapies, offering a therapeutic option for targeting tissues that are contraindicated for surgical resection, thermal ablation, or radiation therapy (4). In light of this important benefit, IRE has shown promising results in the ablation of centrally located hepatic, locally advanced pancreatic, and prostate tumors (5–7).

The formation of nanoscale defects occurs independently of thermally induced processes, and the nonthermal mechanism was demonstrated in a large soft-tissue sarcoma and during an intracranial procedure (8,9). Nonetheless, recent studies (2,3,10,11) have shown that the therapeutic application of IRE will result in secondary Joule heating that can induce thermal damage. Given the fact that the underlying rationale for the clinical application paradigms of IRE are based in large part on the assumption of the nonthermal mechanism of cell death, characterization and quantification of the thermal effects of IRE is necessary to ensure safe but effective ablations (2).

We hypothesize that thermal distribution during IRE ablations varies with respect to the ablation settings depending on the amount of Joules delivered. The heating effects will initially be observed around the needles and will subsequently merge after substantial energy delivery. Additionally, it was hypothesized that sequential pulsing results in less temperature increase than consecutive pulse delivery because of the intermittent cooling periods without Joule delivery. It was also hypothesized that electrolysis of water might occur during IRE pulsing in water-based gel because, by using direct current through an ionic substance, an interchange of ions takes place and causes this effect.

The primary goals of the present study are the visualization of physical effects of IRE pulses, quantification of the development and distribution of thermal energy during IRE using optical approaches, and determination of the influence of different ablation parameters on thermal outcome. The secondary goals are the evaluation of the effect of sequential (pulse delivery interrupted by breaks) versus consecutive pulse delivery and the evaluation of nonparallel electrode placement on thermal effect during IRE. The further identification of the thermal component of IRE is vital for the improved safety of IRE in interventional oncology.

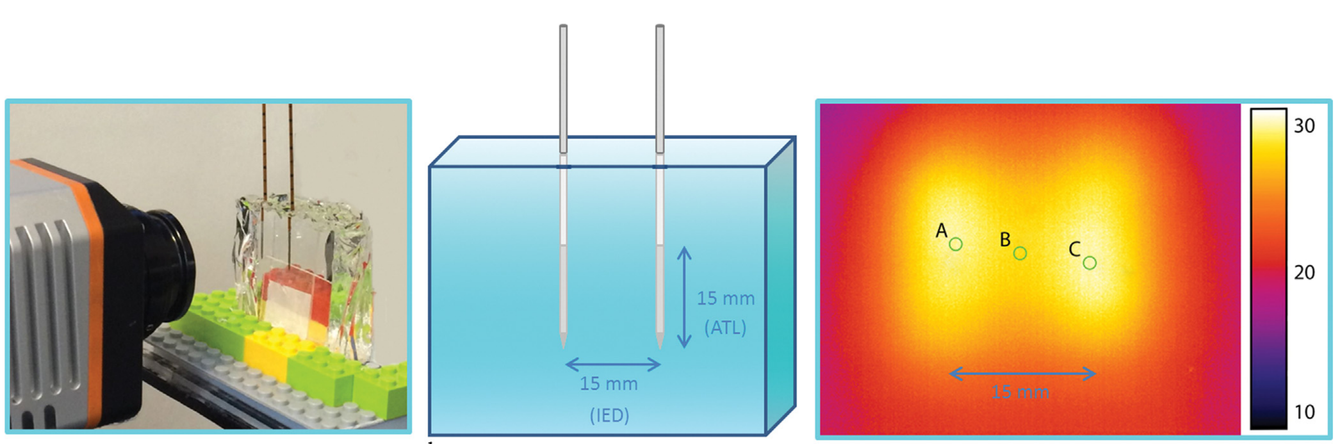
## MATERIALS AND METHODS

### Tissue-Mimicking Gel Phantom

We used a transparent polyacrylamide gel with characteristics that mimic soft biologic tissue with respect to mechanical properties and electrical and thermal conduction (12). For 100-mL gel, we used 60 mL saline solution (NaCl 0.9%), 50 mg ammonium persulfate, 40 mL 30% acrylamide/bis solution, and 80 μL tetramethylethylenediamine. The gels were casted by pouring the liquid material into a fixed mold. Dimensions of the gel were 10 cm in width, 8 cm in height, and 1.5 cm in thickness, which allowed for electrode placement similar to in vivo settings.

### IRE Procedure

The IRE procedure was performed by using the NanoKnife IRE console (AngioDynamics, Latham, New York). For the standard ablation setting, two monopolar 19-gauge needle electrodes were placed exactly parallel in the gel, 5 mm ± 1 from the surface, by using a grid (Fig 1). The proximal aspect of the active tip was constantly approximately 4 cm from the top surface. The default ablation settings were 15-mm interelectrode distance and 15-mm active tip length (ATL), delivering 1 × 90 pulses with a pulse length of 90 μs, 90 pulses per minute, and pulse intensity of 1,000 V/cm. The influence of the following ablation parameters on the temperature was assessed: voltage (ranging from 500 to 2,500 V;




a. b. c.

**Figure 1.** **(a)** Close-up image shows the thermal camera and electrodes inserted in gel. **(b)** Schematic image of the electrodes in the gel with standard settings (interelectrode distance [IED] of 15 mm and ATL of 15 mm). **(c)** Analysis of temperature recordings with three ROIs.