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Original article

Irreversible electroporation of the porcine kidney: Temperature development and distribution

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Abstract

Objective: Although tissue ablation by irreversible electroporation (IRE) has been characterized as nonthermal, the application of frequent repetitive high-intensity electric pulses has the potential of substantially heating the targeted tissue and causing thermal damage. This study evaluates the risk of possible thermal damage by measuring temperature development and distribution during IRE of porcine kidney tissue.

Methods: The animal procedures were conducted following an approved Institutional Animal Ethics Committee protocol. IRE ablation was performed in 8 porcine kidneys. Of them, 4 kidneys were treated with a 3-needle configuration and the remaining 4 with a 4-needle configuration. All IRE ablations consisted of 70 pulses with a length 90 μs. The pulse frequency was set at 90 pulses/min, and the pulse intensity at 1,500 V/cm with a spacing of 15 mm between the needles. The temperature was measured internally using 4 fiber-optic temperature probes and at the surface using a thermal camera.

Results: For the 3-needle configuration, a peak temperature of 57°C (mean = 49 ± 10°C, $n = 3$) was measured in the core of the ablation zone and 40°C (mean = 36 ± 3°C, $n = 3$) at 1 cm outside of the ablation zone, from a baseline temperature of 33 ± 1°C. For the 4-needle configuration, a peak temperature of 79°C (mean = 62 ± 16°C, $n = 3$) was measured in the core of the ablation zone and 42°C (mean = 39 ± 3°C, $n = 3$) at 1 cm outside of the ablation zone, from a baseline of 35 ± 1°C. The thermal camera recorded the peak surface temperatures in the center of the ablation zone, reaching 31°C and 35°C for the 3- and 4-needle configuration IRE (baseline 22°C).

Conclusions: The application of repetitive high-intensity electric pulses during IRE ablation in porcine kidney causes a lethal rise in temperature within the ablation zone. Temperature monitoring should be considered when performing IRE ablation near vital structures.

Keywords: Irreversible electroporation; IRE; Ablation; Temperature; Thermal; Kidney

1. Introduction

Electroporation or electropermeabilization is a technique in which electric pulses between 2 electrodes are used to create "nanopores" in the cell membrane [1,2]. These pores allow molecules to enter the cell. The process can be temporary (reversible electroporation) or permanent (irreversible electroporation [IRE]) based on a certain threshold above which the "nanopores" become permanent causing cell death owing to the inability to maintain homeostasis [3–5]. Reversible electroporation was initially developed for

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intracellular gene and drug delivery [6,7]. In recent years, interest turned to IRE as a tumor ablation modality resulting in the development of commercially available medical equipment [8]. Conceptually, IRE is not dependent on thermal effects for tissue destruction and is therefore not influenced by "thermal sink," promising consistent results near large vessels or the renal collecting system. Furthermore, IRE should be confined to damage of the cell membrane, sparing tissue architecture and minimizing damage to blood vessels, nerves, and other vital structures [9].

It is known that the application of repetitive high-intensity electric pulses has the potential of substantially heating the targeted tissue and in effect causing thermal damage. Lethal cellular damage will occur within 4 to 6 minutes at temperatures above 50°C and almost instantaneously when temperatures exceed 60°C [10]. It is important for clinicians to be aware of temperature development during IRE so that the possible risk of severe thermal damage to vital structures can be minimized.

Data from in vivo experimental studies on thermal effects are limited. Faroja et al. assessed temperature development during IRE of porcine liver, using 1.3-cm diameter flat plate electrodes. Testing varying settings, the temperature reached up to 84°C for 360 pulses of 2,900 V (baseline 34°C) [11]. To aid in treatment planning, van Gemert et al. performed a mathematical temperature simulation based on the electrical and thermal properties of prostate tissue in combination with clinically practiced IRE settings. Using an electrode spacing of 1 cm, the estimated temperatures reached between 92°C and 67°C at a distance 0.5 to 5 mm from the probes [12]. We hypothesize that IRE of porcine kidney using clinically practiced IRE settings will cause heating of the targeted tissue up to lethal levels. On histopathological evaluation of IRE lesions, it is impossible to differentiate accurately between IRE effect and thermal damage. Therefore, knowing at what temperature thermal damage will occur, we have chosen to accurately measure actual temperatures during IRE ablation. The objective of this in vivo animal study is thermal mapping during IRE of porcine kidney, and in doing so, assessing the risk of thermal damage.

2. Materials and methods

2.1. Animal procedure

The animal procedures were conducted following an approved Institutional Animal Ethics Committee protocol. In 4 domestic farm pigs, weighing approximately 60 kg, IRE ablation was performed on both kidneys. The animals were sedated with intramuscular injections of ketamine (10–15 mg/kg), midazolam (1–1.5 mg/kg), and atropine (1.5 ml/50 kg). After intubation, anesthesia was maintained through inhaled isoflurane (0%–4%) and intravenous ketamine (2 mg/kg/h), sufentanil (5–10 μg/kg/h), midazolam (1–2 mg/kg/h), and rocuronium (2–2.5 mg/kg/h). Before IRE, intravenous bolus injections of rocuronium (1–1.5 mg/kg) were administered to achieve sufficient muscular relaxation.

Animals were placed in a supine position. The abdomen was opened through a medial laparotomy incision after which both kidneys were localized and exposed. After the IRE procedure, the pigs were killed and the kidneys harvested for gross examination.

Gross examination consisted of a midline coronal incision, dividing the kidneys into symmetrical halves. The diameter and aspect of the IRE ablation zone were assessed macroscopically.

2.2. IRE procedure

The procedure used the NanoKnife IRE console in combination with 19-gauge monopolar needle electrodes (AngioDynamics Inc., Queensbury, NY). In total, 4 kidneys were treated with 3 electrodes placed in an equilateral triangular formation, spaced 15 mm apart (Fig. 1A). The electrodes were inserted interpolar at a depth of 20 mm with a tip exposure of 15 mm (Fig. 1A). The IRE console was set at 3 × 70 pulses with a length of 90 μs per pulse with a frequency of 90 pulses/min and the pulse intensity set at 1,500 V/cm. Typically, a current of 20 to 40 A runs between the electrodes during the pulse. The IRE console delivers the pulses in trains of 10 pulses, separated by 3.5 seconds of recharging. For experimental purposes, the 3-needle IRE ablations were repeated with the electrodes in the same position. This doubled the IRE exposure, rendering the gross examination to be an overestimation of the ablation effects.

The remaining 4 kidneys were treated with 4 electrodes in a square formation, spaced 15 mm apart (Fig. 1B) and fixed using external spacers (Fig. 2). Again, the electrodes were inserted interpolar at a depth of 20 mm with a tip exposure of 15 mm (Fig. 1B). The IRE ablation consisted of 6 × 70 pulses of 90 μs per pulse at a timing of 90 pulses/min. The pulse intensity was set at 1,500 V/cm.

2.3. Temperature measurements

The temperature was measured within the tissue using fiber-optic temperature probes and at the tissue surface using a thermal camera. The fiber-optic temperature setup consisted of a rack mounted Lumiterm X5 OEM temperature board, connected to 4 Lumiterm X5-True fiber-optic temperature probes with a diameter of 1 mm (Ipitek, Carlsbad, CA). The system is capable of registering 0.05°C temperature differences with an accuracy of 0.25°C. The temperature-recording interval was set at 1 to 4 seconds.

The temperature probes were inserted in the tissue with the use of 16-gauge IV cannulas at a depth of 20 mm (Fig. 2B). The probe tips were at an equal depth to the IRE electrode tips, based on ex vivo experiments in our institution, which showed temperatures to be highest in