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Review Article

Irreversible Electroporation: A Novel Ultrasound-guided Modality for Non-thermal Tumor Ablation

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Abstract Ultrasound-guided tumor ablation techniques have been proven to be highly effective and minimally invasive in the treatment of many diseases. Traditional approaches to ablation include microwave and radiofrequency techniques, cryotherapy, and high-intensity focused ultrasound. However, these methods are prone to heat-sink effects that can diminish the effectiveness of treatment and damage adjacent structures, such as bile ducts, blood vessels, the gallbladder, or bowel. Irreversible electroporation (IRE) is a non-thermal ablation modality that induces cell apoptosis through the application of high-voltage current. IRE is not limited by many of the limitation which affects conventional tumor ablation techniques, and is particularly useful in treating sensitive areas of the body. The article reviews the basics of ultrasound-guided technology, including its clinical applications and effectiveness in the treatment of tumors.

Introduction

Basic rationale

Irreversible electroporation (IRE) is a novel, non-thermal tumor ablation modality [1,2] that delivers ultra-short high-voltage electrical impulses to a target area through fine antennae. The resultant strong external electric field causes electroporation (i.e. causes permeable nanoscale pores to form in the cell membrane) [3—6]. This phenomenon has previously been used in the laboratory to promote intracellular gene delivery. Electroporation can be reversible or irreversible, depending on the electric voltage and pulse length that are applied (Fig. 1) [7]. Lipid bilayer cell membranes are vital cellular structures which regulate intracellular and extracellular solute transport. When the intensity of the induced electric field (determined by the

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voltage and duration of the electric pulse) exceeds a particular threshold, the permeable pores on the cell membrane are opened permanently. This causes the membrane to lose its physiological function by preventing it from returning to a state of homeostasis, which in-turn leads to cell apoptosis and the clearing away of cell debris by the host immune system [2–4]. Potential damage to surrounding healthy tissue is minimized by preventing exposure to extreme cold or heat. Despite the recent advent of IRE, numerous clinical studies have already demonstrated its efficacy as an alternative approach to the treatment of tumors in sensitive areas of the body [8].

Ablation systems and devices

The NanoKnife® IRE System (AngioDynamics, Latham, NY) is an IRE-based ablation system in wide clinical use [9]. As shown in Fig. 2, this system includes a generator and multiple monopolar antennas. IRE ablation should be administered under continuous vital sign monitoring and, to ensure that excitation of the motor neural end-plate does not induce muscle spasms during electroporation, patients should be held in a supine position under general anesthesia and total muscle paralysis [10,11]. Prior to electroportation, imaging guidance techniques (e.g. ultrasound or computed tomography) are used to help position between two to and six antennas, which are placed within the target area by via aseptic manipulation (Fig. 3). Of imaging guidance techniques, ultrasound is particularly effective at providing a clear field in which structures surrounding the tumor can be identified. The percutaneous approach to IRE is minimally invasive and is commonly used in liver tumor ablation; however, this approach is not well suited to sites which are located deeper in the abdomen, such as the pancreas, due to a degraded ultrasound window. In these cases, the laparotomic approach is generally preferable; however laparoscopy may also be technically feasible in highly-selected patients. Nonetheless, intra-operative ultrasound guidance is still necessary when IRE is performed using a surgical approach.

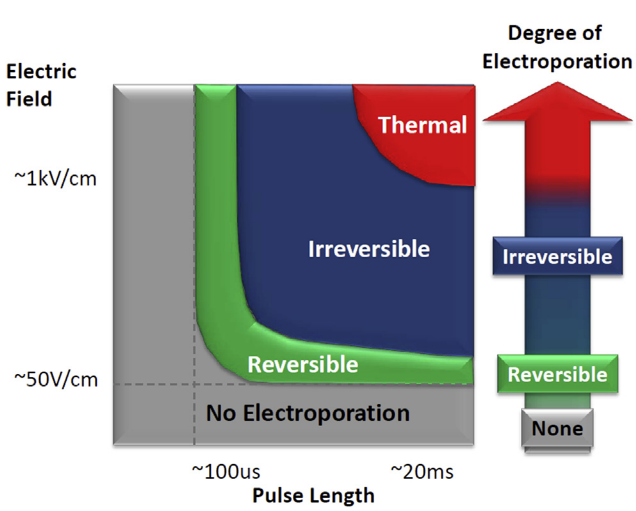

Figure 1 The reversibility of electroporation depends on the intensity of the electric field and the pulse length. Higher voltages and longer pulses cause irreversible electroporation; however, the excessive delivery of electric current can result in local heating rather than electroporation.

Figure 2 The IRE generator includes an electric power supply, a computer, and 6 output ports that are connected to antennae for the delivery of electric current.

The location and size of ablation zone could be estimated by the generator after imputing the information including antenna number, electric power and antenna location (Fig. 4).

The antenna used for IRE is a 19 gauge needle with an active tip and that can be adjusted to the length between 0.5 and 4 cm. The tip includes an echogenic marker, which allows the antenna to be visible under ultrasound examination (Fig. 5). Following antenna placement, ten test pulses are delivered to the target area, and the tissue response to IRE is observed. If the tissue response is satisfactory without abrupt elevation of delivered electric current, then another 80 IRE ablation pulses are administered.

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