Assessment of Various Types of US Findings after Irreversible Electroporation in Porcine Liver: Comparison with Radiofrequency Ablation

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ABSTRACT

Purpose: To assess various ultrasound (US) findings, including B-mode, shear-wave elastography (SWE), and contrast-enhanced US, in accurately assessing ablation margins after irreversible electroporation (IRE) based on radiologic–pathologic correlation, and to compare these findings between IRE and radiofrequency (RF) ablation.

Materials and Methods: IRE (n = 9) and RF ablation (n = 3) were performed in vivo in three pig livers. Each ablation zone was imaged by each method immediately after the procedure and 90 minutes later. Ablation zones were evaluated based on gross pathologic and histopathologic findings in samples from animals euthanized 2 hours after the last ablation. The characteristics and dimensions of the histologic ablation zones were qualitatively and quantitatively compared against each US finding.

Results: In B-mode US at 90 minutes after IRE, the ablation zones appeared as hyperechoic areas with a peripheral hyperechoic rim, showing excellent correlation ($r^2 = 0.905$, $P < .0001$) with gross pathologic findings. SWE showed that tissue stiffness in the IRE ablation zones increased over time. Contrast-enhanced US depicted the IRE ablation zones as hypovascular areas in the portal phase, and showed the highest correlation ($r^2 = 0.923$, $P < .0001$) with gross pathologic findings. The RF ablation zones were clearly visualized by B-mode US. SWE showed that tissue stiffness after RF ablation was higher than after IRE. Contrast-enhanced US depicted the RF ablation zones as avascular areas.

Conclusions: IRE and RF ablation zones can be most accurately predicted by portal-phase contrast-enhanced US measurements obtained immediately after ablation.

ABBREVIATIONS

IRE = irreversible electroporation, NADPH = nicotinamide adenine dinucleotide phosphate, RF = radiofrequency, ROI = region of interest, SWE = shear-wave elastography

Irreversible electroporation (IRE) has been proposed as a promising new tissue ablation technique (1); however, a possible disadvantage of IRE is its lower success rate for complete local tumor eradication (a local recurrence rate of 40% at 12 mo was reported by Cannon et al [2]). This may be attributable to the fact that the optimal timing of image-based follow-up and the most suitable imaging modality for follow-up have yet to be determined because IRE therapy has only recently been introduced, although some studies have already been conducted (3,4).

Ultrasound (US) has been a widely employed imaging modality for guidance, monitoring, and postablation assessment in IRE ablation procedures. Appelbaum et al (5) reported in detail that the ablation zone could

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be best predicted by measuring the external hyperechoic rim that forms at 90–120 minutes in B-mode US images. However, we believe this finding is observed too late to permit repeat intervention if remaining viable tumor is found, and would affect the efficiency of IRE treatment. It is therefore necessary to investigate other promising US-based technologies such as contrast-enhanced US and shear-wave elastography (SWE) that may be useful for immediate intraprocedural monitoring of tissue responses during IRE procedures.

However, to our knowledge, there have been few reports on contrast-enhanced US and SWE imaging for the evaluation of IRE ablation zones after the procedure, even though there have been many reports on these imaging methods for the evaluation of RF ablation (6–8), because thermal ablation techniques such as RF ablation have been time-tested for nearly three decades. In addition, we are aware of no reports directly comparing the imaging and histopathologic differences between nonthermal IRE ablation zones and thermal RF ablation zones.

The present study was therefore conducted with two objectives: (i) to evaluate the acute appearance of IRE ablation zones on B-mode US, contrast-enhanced US, and SWE imaging in a porcine liver model and to compare each against the pathologic findings with size correlation; and (ii) to compare each imaging and histopathologic finding between IRE ablation zones and RF ablation zones.

MATERIALS AND METHODS

Animal Model

Our institutional animal care and use committee approved the animal model used in this study. Three female adult pigs weighing 30–40 kg were purchased from an approved supplier and preconditioned onsite. The animals received proper care by highly qualified staff according to the principles and guidelines established by the animal care and use committee of our university, and were fasted for 12 hours before the procedure. Anesthesia was induced with 32.4 mg/kg of pentobarbital sodium (Somnopentyl; Kyoritsu Seiyaku, Tokyo, Japan) by intramuscular injection and 16.2 mg/kg of pentobarbital sodium by intravenous injection. Anesthesia was maintained with 8.1 mg/kg of pentobarbital sodium by intravenous injection at 1-hour intervals. Vecuronium bromide (1 mg/mL, 0.25 mg/kg; Musculax; Merck, Whitehouse Station, New Jersey) was administered for muscle blockade during the application of IRE energy to eliminate inadvertent muscle stimulation. The liver was accessed via open laparotomy with packing to ensure adequate hepatic exposure.

IRE Procedure

Two monopolar 19-gauge electrodes (AngioDynamics, Latham, New York) were inserted directly into the liver parenchyma at the desired locations with the aim of placing the electrodes 1.3–2.0 cm apart with 2-cm tip exposure. The normal porcine livers used were, on average, less than 4–5 cm thick in most segments, and the probes were therefore located 2–4 cm deep in the liver parenchyma. US guidance was used to select regions of solid parenchyma. In addition, the electrodes were placed with a minimum of 5 cm between each zone of coagulation to minimize potential effects of earlier trials on subsequent ablation. The electrodes were then connected to an electroporation generator (NanoKnife; AngioDynamics). Energy deposition was performed at 1,950–3,000 V (pulse length, 70–100 μs; number of pulses, 90; and total pulses delivered, 90–270). These IRE parameters were based on the standard clinical parameters recommended by the manufacturer, and only the total pulses delivered was varied to obtain different IRE ablation sizes (90 pulses in group 1, 180 pulses in group 2, and 270 pulses in group 3). IRE ablation was performed in three areas of the liver in each pig. In total, nine IRE ablation zones were created.

RF Ablation Procedure

Two bipolar RF electrodes (2.0-cm tip exposure; Celon-ProSurge; Olympus Winter and Ibe, Hamburg, Germany) with 1.0-cm spacing were inserted directly into the liver parenchyma in the same manner as for IRE. The electrodes were connected to an RF generator (Celon-POWER System; Olympus Winter and Ibe). In this system, internal liquid circulation in the applicator allows the efficiency of coagulation to be increased, with liquid flow provided by a peristaltic pump included in the system. The output power and total energy in each session were fixed at 40 W and 15 kJ, respectively, according to the recommendations of the manufacturer. RF ablation was performed on one area of the liver in each pig. In total, three RF ablation zones were created.

B-Mode US Imaging and Measurements

Intraoperative B-mode US scans were obtained by two hepatologists (F.M. and Y.K., with 25 and 15 y of experience, respectively, in standard US and contrast-enhanced US). The US equipment used was a TUS-A500 (Aplio 500; Toshiba Medical Systems, Otawara, Japan) with a 6.0-MHz linear transducer (PLT-604AT; Toshiba Medical Systems). Images were saved as grayscale axial and longitudinal images.

The US findings for each ablation zone were characterized based on the consensus of the two hepatologists with regard to echogenicity (which was classified as hypoechoic, isoechoic, hyperechoic, or unclear in comparison with surrounding liver parenchyma) and dimensional measurements. All US images were analyzed by using a dedicated workstation (UltraExtend FX; Toshiba Medical Systems). B-mode US was performed