BTX Applications

Tech-Trends
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Irreversible electroporation/tissue ablation in rat liver

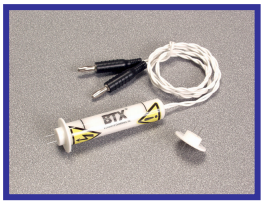
Irreversible Electroporation Therapy in the Liver: Longitudinal Efficacy Studies in a Rat Model of Hepatocellular Carcinoma

Background:
Irreversible electroporation (IRE) is an innovative local-regional therapy that involves delivery of intense electrical pulses to tissue to induce nanoscale membrane defects for tissue ablation. The purpose of this study was to investigate the feasibility of using IRE as a liver-directed ablation technique for the treatment of hepatocellular carcinoma (HCC).

Methods:
In the N1-S1 rodent model, hepatomas were grown in 30 Sprague-Dawley rats that were divided into treatment and control groups. For treatment groups, electrodes were inserted and eight 100 µs 2500 V pulses were applied to ablate the targeted tumor tissues. For both groups, magnetic resonance imaging scans were performed at baseline and 15-day follow-up intervals to determine tumor sizes as a tactic to assess longitudinal outcomes.

Results:
MR images showed a significant tumor size reduction within 15 days post therapy, and histology correlation studies showed a clear progression from poorly differentiated viable hepatoma tissue pretherapy to extensive tumor necrosis and complete tumor regression in 9 of 10 treated rats 7 to 15 days after treatment.

Conclusions:
This preclinical study showed the feasibility of using IRE as a novel ablation modality for targeted treatment of hepatoma in the N1-S1 rat model. Follow-up MRI images showed significant tumor size reductions and histology correlation studies showed extensive tumor necrosis within 7 to 15 days post therapy. IRE is a promising new approach for liver-directed treatment of HCC and may offer multiple potential benefits over conventional ablation methods.



ECM 830 Electroporator Cat. 450002
10 mm 2-Needle Array Cat. 450167

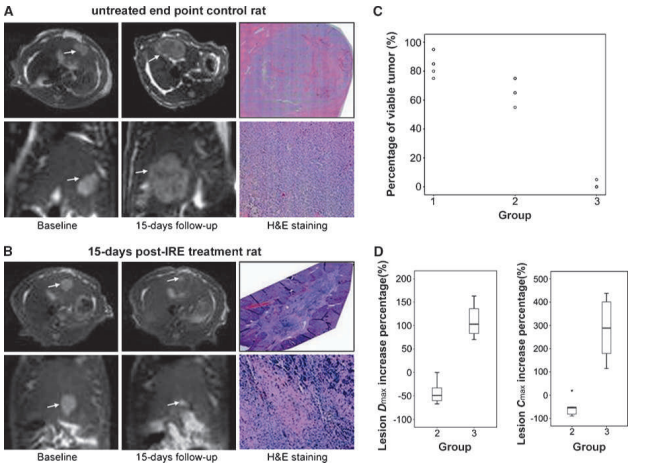


Fig. 4. Axial- and coronal-orientation MRI images along with corresponding pathologic H&E slide images for an untreated 15-d end point control rat (A) and a 15-post-IRE treatment rat (B). Notice the significant increase in tumor size for the untreated rat (A) compared with the notable tumor size reduction for the IRE-treated animal (B). Arrows indicate tumor positions. H&E pathology slides showed 70% viable tissue within the untreated tumor (A). And completed tumor regression within the IRE-treated rat (B). Scatter plot © shows the pathology-confirmed percentage of viable tumor tissue for six rats at baseline control interval (group 1), six untreated control rats following a 15-d growth period after original baseline scan (group 2), and six IRE-treated rats following the 15-d growth period (group 3). Box plots (D) show the lesion D_{max} increase (left) and C_{max} increase (right) for 15-d follow-up animals in untreated control group 2 and IRE-treated group 3. The boundary of the boxes closest to zero indicates 25th percentile, line within boxes show median, and boundary of boxes furthest from zero indicates 75th percentile. Outliers are represented as stars. D_{max} and C_{max} increases for group 2 rats were significantly greater than D_{max} and C_{max} increases for group 3 rats (P=0.004 for both comparisons using nonparametric Mann-Whitney U test.

ECM 830 IRREVERSIBLE ELECTROPORATION (IRE)/TISSUE ABLATION PROTOCOL

Cell Preparation:
N1-S1 rat hepatoma cell line (ATCC) was obtained and cultured in DMEM supplemented with 10% fetal bovine serum (Sigma-Aldrich) and 90 µg/ml gentamicin. Cells were maintained in suspension culture flasks at 37ºC in a humidified atmosphere containing 5% CO_2. This cell line was originally established from a HCC induced male Sprague-Dawley rat by ingestion of carcinogen 4-dimethylaminoazobenzene. Before each implantation procedure, the viability of the cells was tested with trypan blue staining (confirming >90% cell viability for each tumor implantation procedure). Rats were anesthetized with a high limb injection of ketamine (75-100 mg/kg) and xylazine (2-6 mg/kg).

Electroporation Settings:

Choose Mode:	HV
Set Voltage:	2500 V
Set Pulse Length:	100 µs
Set Pulse Number:	8
Pulse Interval:	100 millisec
Electrode Gap:	10 mm
Post Treatment:	Following IRE, abdominal incisions were closed with two-layer technique followed by topical application of antibiotic ointment and Metacam injection.

Electroporation Protocol:

Temp:	Room Temperature
Pulse:	Press Start to Activate Automatic Pulse/Charge Sequence

References:
Yang Guo[1], Yue Zhang[1,2], Rachel Klein[1], Grace M. Nijm[6], Alan V. Sahakian[6], Reed A. Omary[1,3,4], Guang-Yu Yang[3,5], and Andrew C. Larson[1,2,3,4,6]
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