Can T1 or T2-Weighted MRI Measurements Detect Irreversible Electroporation Ablation Zones in Liver Tumors?

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INTRODUCTION

Irreversible electroporation (IRE) [1] has been applied as a novel tissue ablation modality; IRE involves application of short-lived electrical fields across the cell membrane to permanently increase membrane permeability leading to cell death. MRI measurements have been used to intra-procedurally monitor tissue response immediately after IRE in normal hepatic parenchyma [2]. The purpose of this study was to determine whether conventional T1- or T2-weighted MRI measurements are similarly effective for monitoring tissue response in liver tumors using the rodent N1-S1 hepatoma model.

MATERIALS AND METHODS

MRI Measurements ACUC-approved studies were performed using N1-S1 HCC Sprague-Dawley rats (N=6). All pre- and post-IRE imaging scans were performed using a 3T clinical MR scanner (Siemens Trio) with 4-element carotid array coils. We acquired pre-IRE T1-weighted (T1W) GRE images with TR/TE = 200/2.5ms, flip angle = 90°, bandwidth = 500 Hz/pixel, T2-weighted (T2W) TSE images with TR/TE = 3640/61ms, flip angle = 150°, bandwidth = 205 Hz/pixel and inversion recovery (IR) images with TI = 400ms (IR_{400}, to null the signal of normal liver) and 800ms (IR_{800}, to null the signal of tumor). *IRE Procedures* After pre-IRE scans, rats were removed from the scanner bore. Liver was exposed and electrodes were inserted into the liver to straddle tumor centroid. 2kV square wave pulses were applied (8 pulses, 100 µs for the duration of 1pulse and 100ms interval between pulses). Immediately after IRE, animals were returned to the scanner bore for post-IRE MRI scans. *Histology and Data Analysis* After post-IRE scans, rats were survived for 24 hours and euthanized to harvest liver. Liver specimens were fixed in formalin and stained using hematoxylin and eosin (H&E). ImageJ (NIH) was used to manually draw a region-of-interest (ROI) circumscribing areas of cellular necrosis within each image to measure the resulting ablation zone for each animal. ROIs were also drawn to measure the MRI signal change zones separately within T1W, T2W, IR_{400} and IR_{800} images. Relative signal to noise ratio (SNR) for normal liver and tumor before and after IRE for the 4 imaging contrasts were measured and compared. *Statistical Analysis* Pearson's correlation and Lin's concordance coefficients were used to determine the relationship between MRI signal change zone and histology-confirmed ablation zone and Bland-Altman plots were generated to investigate the agreement of two measurements. *T*-test was performed to compare the difference of SNRs before and after IRE in normal liver and within tumor tissues ($p<0.05$ considered statistically significant).

RESULTS

Fig.1 shows pre- and post-IRE images. Ablated normal liver were observed as hypo-intense on T1W (**Fig.1C**), hyper-intense on T2W and IR_{400} (**Fig.1D**), images. The signal change within tumor cannot be visualized within 4 imaging contrast, which was demonstrated by **Fig.2**: the SNR of ablated normal liver was significantly different from pre-IRE normal liver within T1W (p=0.003), T2W (p=0.004) and IR_{400} images (p=0.125); but SNRs of tumor before and after IRE were not significantly different (p=0.056 for T2W, p=0.125 for IR_{400} and p=0.922 for IR_{800}). MRI signal change zones were correlated to histology-confirmed ablation zones (r=0.671, p=0.114 for T1W; r =0.860, p=0.028 for IR_{400}), but show poor concordance (r_c=0.027 for T1W, r_c=0.031 for IR_{400}). All histological measurements are larger than MRI signal change zone, as shown in the Bland-Altman plots in **Fig.3**.

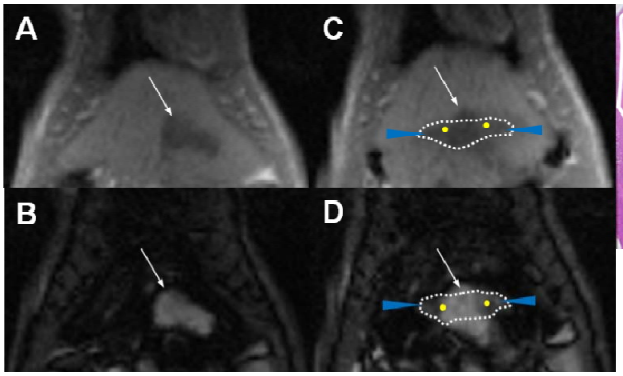
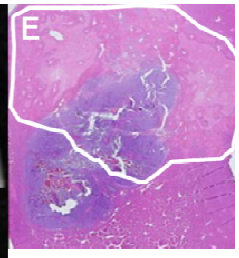


Fig 1. Pre-IRE (**A,B**), post-IRE (**C,D**) and histology H&E (**E**) images of ablation zone within an N1S1 tumor. Signal change was observed in surrounding normal liver tissue (blue arrows) but not in tumor (FEM-based anticipated ablation zone shown with dashed line). H&E shows upper portion of tumor was ablated (**E**) even though no MRI signal changes were observed.



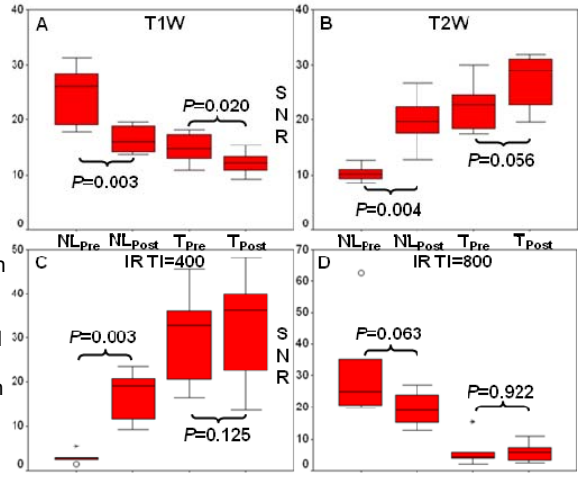


Fig 2. (right). Signal in ablated normal liver changed post-IRE, while signal for treated tumor tissues showed little alteration for each of the four acquisition methods (NL: normal liver; T: tumor).

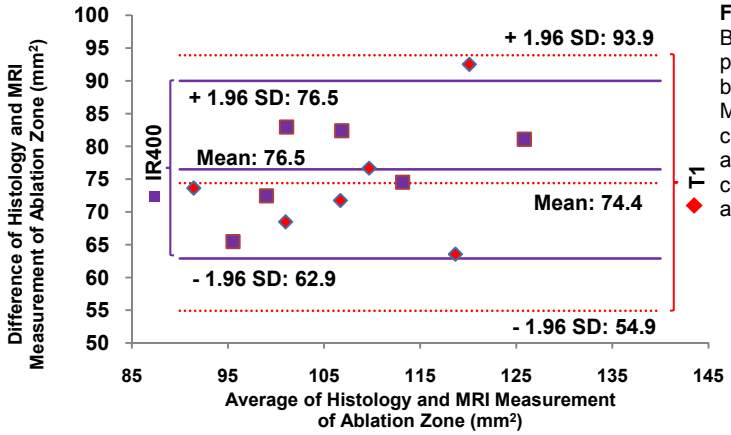


Fig 3. (**left**) Bland-Altman plots show bias between MRI signal change zones and histology-confirmed IRE ablation zones.

CONCLUSION While effective for visualization of IRE ablation zones in normal hepatic parenchyma [2], conventional T1W, T2W and IR MRI measurements are poorly reflective of IRE ablation zones in tumor tissues. In normal tissues, these signal changes are likely due to fluid extravasation and accumulation upon electroporation. However, within hypovascular N1S1 tumor tissues, such effects may be diminished providing one possible explanation for the current findings. Future studies are necessary to develop new imaging approaches better able to specifically detect signal alterations due cell membrane permeablization in targeted tumor tissues.

Reference: [1]. Rubinsky et al. Technol Cancer Res Treat 2007;6:37-48
[2]. Zhang et al. Radiology 2010;256(2):424-432

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