In Vivo Diffusion-Weighted Imaging of Liver Tumor Necrosis in the VX2 Rabbit Model at 1.5 Tesla

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Introduction:

Decreased cellularity and compromised cell membrane integrity in necrotic tissue allows locally increased translational Brownian motion of water molecules. Diffusion weighted imaging (DWI) techniques exploit this property to permit differentiation of viable and necrotic tumor tissues [1,2]. Previous work at 4.7T demonstrated that DWI can detect cell death following chemoembolization of liver tumors in a VX2 rabbit model post-euthanasia [3]. However, to use these techniques for longitudinal assessment of novel tumor treatment regimens, DWI must be performed *in vivo*. In this study, we tested the hypothesis that *in vivo* DWI can detect liver tumor necrosis in the VX2 rabbit model using a 1.5T clinical MR scanner.

Methods:

In this ACUC-approved study, we implanted VX2 carcinoma cells at multiple positions within the left liver lobe of 3 New Zealand white rabbits. Rabbits were followed for 2-4 weeks to allow tumor growth prior to imaging. Via femoral access under x-ray guidance, we placed a 2-F catheter in the hepatic artery for intraarterial injection of contrast agents. Rabbits were intubated for isofluorane anesthesia and breath-holding using a small animal ventilator (Harvard Apparatus, Holliston, MA). We subsequently imaged rabbits in the supine position using a 1.5T Magnetom Sonata clinical MR scanner (Siemens Medical Solutions, Erlangen, Germany).

Single-shot axial DW-EPI images of the liver were acquired during breath-hold using the following imaging parameters: TR/TE = 3000/1000 ms, 4 mm slice thickness, 750 Hz/pixel BW, non-selective fat saturation, twice refocused spin-echo DW to reduce eddy-current induced distortion [4] with three b-value weightings (0,700,1400 mm^2/s), 200x100 mm^2 FOV, 128x64 matrix (1.6x1.6x4.0 mm^3 voxel size), 4 slices acquired during each 15-s breath-hold. For additional morphological characterization of tumors, dynamic contrast enhanced GRE imaging was performed after intraarterial injection of 2mL of 20% Gd-DTPA solution (Berlex Magnevist) at 0.3 mL/s using the following imaging parameters: TR/TE = 22.5/1.5 ms, 5 mm slice thickness, 200x100 mm^2 FOV, 256x134 matrix, 70° flip angle, 6 interleaved slices sampled repeatedly every 2.1-s for 4 min following contrast injection.

After removal from the scanner bore, we euthanized each rabbit for subsequent necropsy. We harvested livers and stained tumor sections using hematoxylin and eosin (H&E) to confirm tumor necrosis. Apparent diffusion coefficient (ADC) maps were reconstructed from the DW images. ROI were drawn within regions of viable and necrotic tissues in each ADC map that included tumor tissue. Necropsy specimens were used as the standard of reference. Mean ADC values were compared using a two-tailed *t*-test with $\alpha = 0.05$.

Results:

We imaged 6 liver tumors (1.1-3.0 cm diameter) in 3 rabbits *in vivo* while breath-holding using DW-EPI. No motion artifacts were observed in the DW images. ADC values in necrotic tissues, $1.23\pm0.10\times10^{-3}$ mm^2/s, were significantly higher than those in viable tumor tissues, $0.70\pm0.069\times10^{-3}$ mm^2/s (mean±SD, $p<0.05$), with necrotic tumor cores clearly depicted in both DW images and ADC maps. A representative dynamic CE image, ADC map, and tumor necropsy image from a single rabbit are shown in **Fig. 1**.

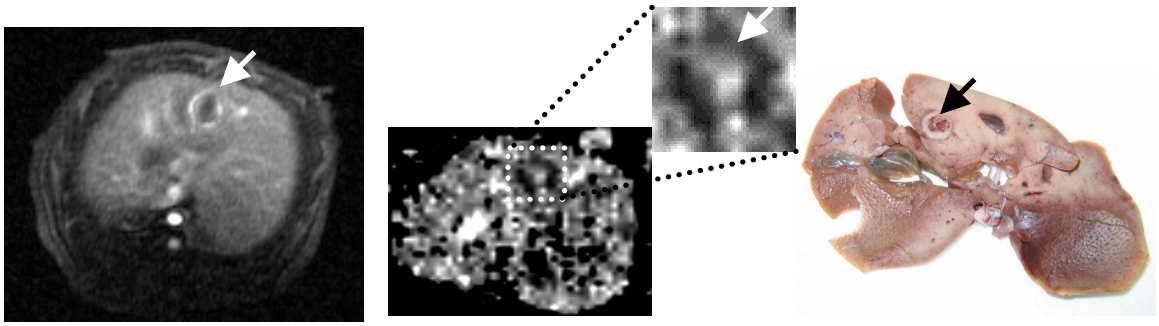

Figure 1. Contrast enhanced image (A), ADC map (B), and necropsy image (C) from a VX2 rabbit with liver tumor position indicated by the arrow in each image. Notice the necrotic core depicted in the ADC map and necropsy image.

Conclusions:

DWI of liver tumor necrosis in the VX2 rabbit model using a 1.5T clinical scanner is feasible *in vivo*. This approach might offer significant utility in the longitudinal assessment of novel hepatocellular carcinoma treatment techniques and MRI-guided interventional therapies.

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[4] Reese et al. Magn Res Med 2003 49(1):177-182