Diffusion-Weighted MRI for Determination of Hepatocellular Carcinoma Response to Yttrium-90 Radioembolization

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Introduction:

Hepatocellular carcinoma (HCC) is the fourth leading cause of cancer death in the United States. Yttrium-90 radioembolization is an emerging HCC treatment that delivers internal radiation to lesions via catheter-directed intra-arterial administration of ^{90}Y microspheres [1]. HCC patients receiving ^{90}Y therapy may be candidates for repeat ^{90}Y administration and/or additional chemoembolization therapies, but detecting maximal tumor response using conventional contrast-enhanced MRI and/or CT requires waiting 3 months after therapy [2]. Therefore, early, non-invasive, biomarkers for predicting response to ^{90}Y therapy could greatly benefit HCC patients. Tumor size changes are the traditional criteria used to non-invasively assess HCC response, but may not correlate with therapeutic efficacy [3,4]. Recent studies have demonstrated that quantitative diffusion-weighted MRI (DW-MRI) may provide sensitive clinical biomarkers for the early stratification of therapy response in brain tumors and breast metastases [5,6]. However, no studies have validated DW-MRI detection of water mobility changes in HCC tissue after ^{90}Y radioembolization. The purpose of this study was to test the hypothesis that DW-MRI can detect increased water diffusion secondary to HCC tissue alteration following ^{90}Y therapy.

Methods:

Superselective ^{90}Y radioembolization (TheraSphere, MDS Nordion, Kanata, ON, Canada) was performed in 5 HCC patients (etiology: 1 NASH, 4 Hep-C, Child-Pugh: 2A, 2B, 1C). For each patient, anatomic and DW-MRI was performed before and ~40 days after ^{90}Y therapy. All imaging was performed using a Magnetom Sonata 1.5T clinical MR scanner (Siemens Medical Solutions, Erlangen, Germany) and flexible six-channel phase-array abdominal imaging coil. Anatomic MRI consisted of T2-weighted HASTE and contrast-enhanced T1-weighted spoiled-GRE with fat-suppression, in the arterial and venous phases. DW-MRI was performed using single-shot spin-echo EPI with scan parameters: TR/TE = 2500/82 ms, slice thickness/gap = 8/4mm, bandwidth = 1.5 kHz/pixel, partial Fourier factor = 6/8, non-selective fat saturation, twice refocused spin-echo diffusion weighting to reduce eddy-current induced distortion with b=0 and 500 s/mm^2. Apparent diffusion coefficient (ADC) maps were reconstructed from each series of DW images. With reference to T1-weighted contrast enhanced images, region-of-interest (ROI) were drawn to measure mean tumor ADC values. We compared mean tumor ADC values before and after ^{90}Y radioembolization (matched pair t-test with $\alpha = 0.05$).

Results:

Tumor ADC increased significantly following ^{90}Y TheraSphere administration; post-therapy tumor ADC increased by $0.87\pm0.57\times10^{-3}$ mm^2/s (mean±SD, $p<0.05$) with pre-treatment ADC = $1.36\pm0.32\times10^{-3}$ and post-treatment ADC = $2.23\pm0.35\times10^{-3}$ mm^2/s. A representative contrast-enhanced image and corresponding ADC map are shown in Fig. 1. In this example, the periphery of the larger tumor (lower) showed regions of low water mobility within the viable periphery (dark outer rim in ADC map) while the core of the tumor demonstrated increased water mobility likely corresponding to necrotic region. Pre- and post-therapy T2-weighted HASTE, contrast-enhanced, and diffusion-weighted (b=500 s/mm^2) images of an HCC patient with left lobe tumor are shown in Fig. 2. HCC conspicuity was relatively poor in most T2-weighted images with no significant changes in signal intensity following therapy. Contrast-enhanced T1-weighted images typically showed peripheral enhancement corresponding to perfused viable regions of HCC lesions. For the left lobe HCC in Fig. 2, the contrast enhancement pattern was very similar before and after ^{90}Y therapy while the diffusion-weighted images demonstrated significant water mobility changes within the core of the tumor after therapy

Conclusion:

DW-MRI can detect increased water diffusion secondary to HCC tissue alteration following ^{90}Y therapy. DWI is a promising technique for non-invasively assessing tumor response to radioembolization. Future studies are necessary to correlate the time course of ADC changes with HCC therapy response and additional technical developments are necessary to improve diffusion-weighted image quality and spatial resolution.

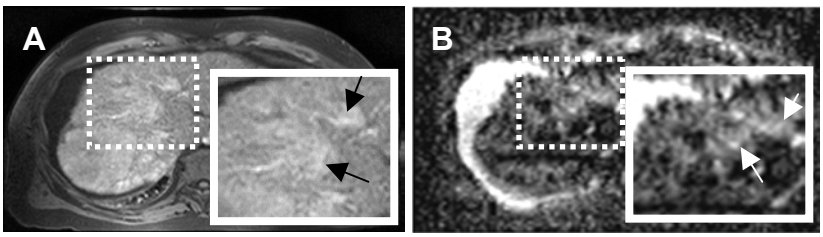

Figure 1. Pre-therapy HCC patient contrast enhanced GRE image (A) and corresponding DW-EPI ADC map (B). Magnified ROI (dashed-box) illustrate tumor positions (arrows). Notice the regions of reduced water mobility at the tumor periphery (viable tissue) as opposed to the relatively high ADC value at the center of the tumor.

[1] Salem et al. J Vasc Interv Radiol 2002 13(9 Pt 2):S223-9
[2] Salem et al. J Vasc Inverv Radiol 2005 *in-press*
[3] Santis et al. J Comput Assist Tomogr 1993 17:901-908.
[4] Ebied et al. Cancer 2003; 97:1042-1050.
[5] Moffat et al. PNAS 2005 102(15):5524-29.
[6] Theilmann et al. Neoplasia 2004 6(6):831-37.

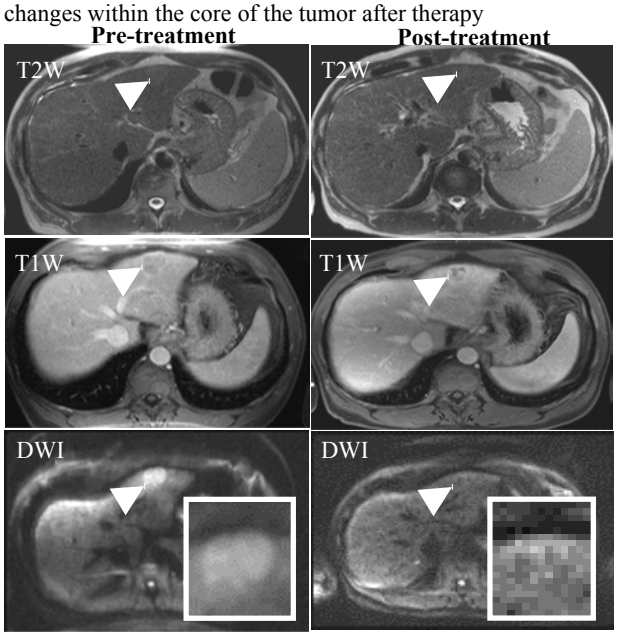

Figure 2. T2-weighted HASTE, contrast-enhanced T1-weighted GRE, and diffusion-weighted (b=500 s/mm^2) images of HCC patient with left lobe lesion (arrows). Notice the increased water mobility within the core of the lesion following ^{90}Y therapy illustrated in the magnified ROI (solid-box).