

# Monitoring therapeutic effect of a vascular disrupting agent: correlation between perfusion parameters derived from intravoxel incoherent motion diffusion-weighted imaging and dynamic contrast enhanced MRI

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**Target Audience:** Radiologists and radiology residents and fellows.

**Purpose:** To evaluate the correlation between serially measured intravoxel incoherent motion (IVIM) diffusion-weighted imaging (DWI) parameters and dynamic contrast enhanced (DCE) MRI parameters for quantitative assessment of therapeutic efficacy of a vascular disrupting agent (VDA) (CKD-516) using rabbit VX2 liver tumors.

**Methods:** The institutional animal care and use committee approved this study. In 15 VX2 liver tumor-bearing rabbits (12 in the treated group and 3 in the control group), IVIM-DWIs using 12  $b$  values from 0 to 800 sec/mm<sup>2</sup> and DCE-MRIs were at a 3T scanner before (baseline), 4 hours, 24 hours, and 7 days after CKD-516 administration. Perfusion-related IVIM-DWI parameters of the tumors including pseudo-diffusion coefficient ( $D^*$ ) and perfusion fraction ( $f$ ) and DCE-MRI parameters including volume transfer coefficient ( $K^{trans}$ ) and initial area under the gadolinium concentration-time curve until 60 seconds (iAUC) were measured. Correlation analysis was performed between IVIM-DWI parameters and DCE-MRI parameters for each time point at baseline and 7 day follow-up using Pearson's correlation analysis. In addition, in the treated group, correlation analysis was performed between the serially measured perfusion-related IVIM-DWI parameters and DCE-MRI parameters of tumors using a linear mixed model for the longitudinal data from baseline to 7 day follow-up.

**Results:** Between the tumor perfusion parameters derived from IVIM-DWI and DCE-MRI both at baseline and 7 day follow-up, no significant correlations were found ( $P>0.05$ ). In the CKD-516 treated group, perfusion-related IVIM-DWI and DCE-MRI parameters significantly decreased at 4 hour follow-up and recovered at 24 hour follow-up. For the longitudinal data in the CKD-516 treated group,  $D^*$  showed significant correlation with  $K^{trans}$  and iAUC, and  $f$  also showed significant correlation with iAUC ( $P<0.05$ ).

**Discussion:** In our study, for evaluation of the perfusion characteristics of liver tumors, parameters of IVIM-DWI and DCE-MRI showed no significant correlation since IVIM-DWI and DCE-MRI may reflect different aspects of tumor perfusion. However, in the longitudinal data after VDA treatment, perfusion-related IVIM-DWI parameters showed significant correlation with DCE-MRI parameters. As VDA's therapeutic effect usually occurs within a few hours, perfusion change should be evaluated within a short time interval. Considering that there is no necessity of a contrast medium for IVIM-DWI, this method could be applicable repetitively which is a big advantage over DCE-MRI. Therefore, our results which showed significant correlation between serially measured IVIM-DWI and DCE-MRI parameters in the VDA treated group suggested that IVIM-DWI can be a useful surrogate of DCE-MRI in the longitudinal monitoring the therapeutic efficacy of VDAs.

**Conclusion:** In the monitoring of tumor perfusion change in response to VDA treatment, perfusion-related parameters derived from IVIM-DWI showed significant correlation with DCE-MRI.

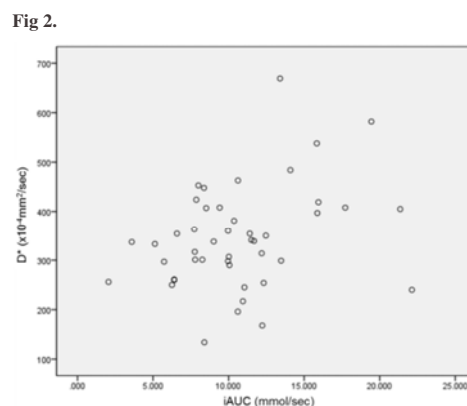
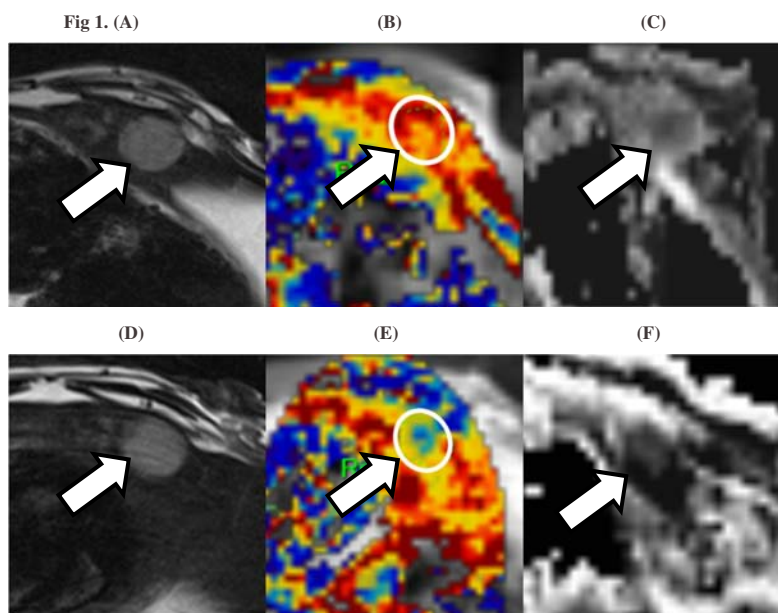


Figure 2. Graph demonstrating the correlation between serially measured iAUC and  $D^*$  in the CKD-516 treated group. A significant positive relationship is observed ( $P<0.05$ ).

Figure 1. Changes of perfusion-related DCE-MRI and IVIM-DWI parameters after CKD-516 treatment. (A-C) T2-weighted axial image, iAUC map from DCE-MRI, and perfusion fraction map from IVIM-DWI at baseline show liver VX2 tumor with iAUC of 16.8 mmol/sec and perfusion fraction of 23.1%. (D-F) Four hours after CKD-516 treatment, perfusion parameters of liver VX2 tumor markedly decreased with iAUC of 10.0 mmol/sec and perfusion fraction of 7.5%.