Intravoxel Incoherent Motion Diffusion Weighted Imaging(IVIM-DWI) on a mouse xenografts model of human nasopharyngeal carcinoma CNE-2 cell line: A preliminary study on 3.0T MRI

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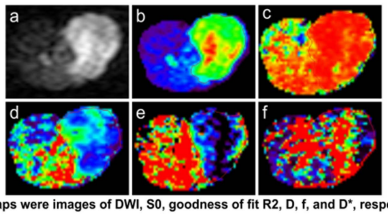
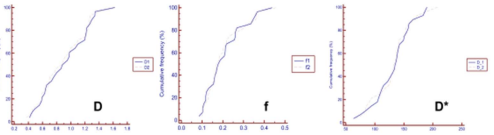
Target audience Radiologists and engineers who are interesting in IVIM-DWI and mouse xenograft model imaging. **Purpose** To preliminarily assess the feasibility of intravoxel incoherent motion diffusion weighted imaging (IVIM-DWI) on mouse nasopharyngeal carcinoma(NPC) xenografts model. **Methods** IVIM-DWI with 14 b-factors (0~1000 s/mm^2) performed on a 3.0T MR system (Achieva, Philips Healthcare, Best, The Netherlands) was conducted on 14 nude mouse NPC xenografts models of CNE-2 cell line. A specialized 4-channel mice coil was applied for IVIM imaging. The IVIM-derived parameters (D, pure diffusion coefficient; f, perfusion fraction; and D*, pseudo-diffusion coefficient) were calculated on xenografts and contralateral normal muscles, respectively, by two experienced radiologists separately on IDL6.3 software(Boulder, Chicago, USA). Interclass coefficient of variation (ICC) were used to test the measurement reproducibility. The IVIM-derived parameters were then compared by Mann-Whitney U test. ROC analysis were then applied to estimate the prognosis tolerance. All statistical analysis were performed on SPSS 18.0(Chicago, IL, USA). **Results** The inter-observer ICCs of xenografts and normal muscles were D (0.97 *vs.* 0.99), D* (0.94 *vs.* 0.97), f (0.96 *vs.* 0.98) and S_0 (0.99 *vs.* 0.99), and their coefficient of variations(CVs) were D (7.35% *vs.* 5.84%), D* (15.08% *vs.* 8.35%), f (6.22% *vs.* 6.10%) and S_0 (7.51% *vs.* 8.69%), respectively. Xenografts presented a significantly higher signal intensity than normal muscles(S_0, 1.25 *vs.* 0.33, $\times 10^4$; P<0.001), even a higher D (1.06 *vs.* 0.785, $\times 10^{-3}$mm^2/s; P=0.035) and a lower f (0.15 *vs.* 0.27; P=0.001). Whereas no significant difference was demonstrated on D* (140.28 vs. 124.55, $\times 10^{-3}$mm^2/s; P=0.178). The ROC analysis indicated that the optimal diagnostic thresholds of D and f value were 0.878 $\times 10^{-3}$ mm^2/s and 0.160, and their corresponding AUC(sensitivity and specificity) were 0.736(0.75, 0.714) and 0.883(0.929, 0.643), respectively. **Discussion** The IVIM model allows the estimation of diffusion and perfusion characteristic simultaneously, and enables derivation of quantitative parameters that separately reflect tissue's diffusivity and microcapillary perfusion[1] without any contrast agent. In this present study, IVIM-DWI was successfully conducted on all of the mouse NPC xenografts model with excellent image qualities as well as considerable inter-observer ICCs and CVs of IVIM parameters, which indicated that IVIM-DWI on 3.0T MRI with a 4-channel mice coil could be feasible in characterizing the diffusion and perfusion features for NPC xenografts. *Kim S et al.*[2] even applied IVIM imaging successfully on mouse mammary carcinoma model and found that the pseudo-diffusion behaved an inverse correlation with interstitial fluid pressure(IFP). In addition, the capability of D and f value were more reliable in differentiating diagnosis in this study, as was in accordance with many previous studies[3,4]. Xenografts with larger areas of stromal tissues appeared to exhibit a higher D value than muscles. While f value is often affected by T2 of tissues or neoplasm[3], and longer T2 of xenografts resulted in a lower f value. In addition, D* value was mainly influenced by the way of measuring region of interest(ROI), and its relatively poor reproducibility was not uncommon as it was reported previously[3,4]. **Conclusion** IVIM-DWI derived parameters are feasible in assessing diffusion and perfusion characteristics for human NPC xenografts of CNE-2 cell line, and NPC xegnografts own a higher D as well as a lower f value.



a-f maps were images of DWI, S0, goodness of fit R2, D, f, and D*, respectively.



The ICCs of D, f and D* parameters of xenograft are 0.97,0.96 and 0.943, respectively.

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